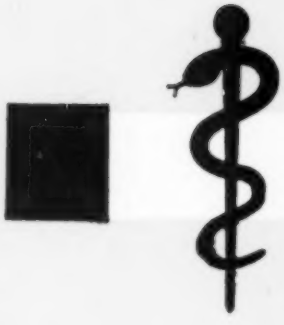
Medical TIMES

THE JOURNAL OF GENERAL PRACTICE



VOL. 81 DECEMBER 1953 NO. 12

a *real* advance in control of

rheumatic pain and spasm

greater predictability • greater safety

mephosal®

mephenesin "solubilized"* by sodium salicylate

MEPHOSAL (capsules, tablets, elixir) combines the safe, skeletal-muscle relaxant mephenesin *made freely soluble* by the primary rheumatic analgesic, sodium salicylate—and thus *more readily available*. The result is *predictable*, faster relief from pain and spasm in over 70% of rheumatic patients as against 55% with salicylates alone, and unpredictable relief with comparatively insoluble mephenesin alone.

IMPORTANT—now 3 dosage forms of **MEPHOSAL**—for greater flexibility and convenience.

MEPHOSAL CAPSULES
Broad range, general rheumatic therapy

Each capsule contains:
Mephenesin . . . . . 250 mg.
Sodium Salicylate . . . . . 250 mg.
(does not contain homatropine methylbromide)
Dose: 1 or 2 capsules every 3 or 4 hours.

MEPHOSAL TABLETS
For rheumatic cases with associated g.i. disturbance

Each tablet contains:
Mephenesin . . . . . 125 mg.
Sodium Salicylate . . . . . 125 mg.
Homatropine Methylbromide . . . . . 1.25 mg.
Dose: 2 or 3 tablets every 3 or 4 hours.

MEPHOSAL ELIXIR
For rheumatic cases with associated g.i. disturbance

Each teaspoonful (4 cc.) contains:
Mephenesin . . . . . 400 mg.
Sodium Salicylate . . . . . 400 mg.
Homatropine Methylbromide . . . . . 2.5 mg.
Dose: 1 teaspoonful every 3 or 4 hours.

Special note: MEPHOSAL TABLETS and MEPHOSAL ELIXIR both contain homatropine methylbromide.

All dosage forms should be given preferably after meals or with a little milk.

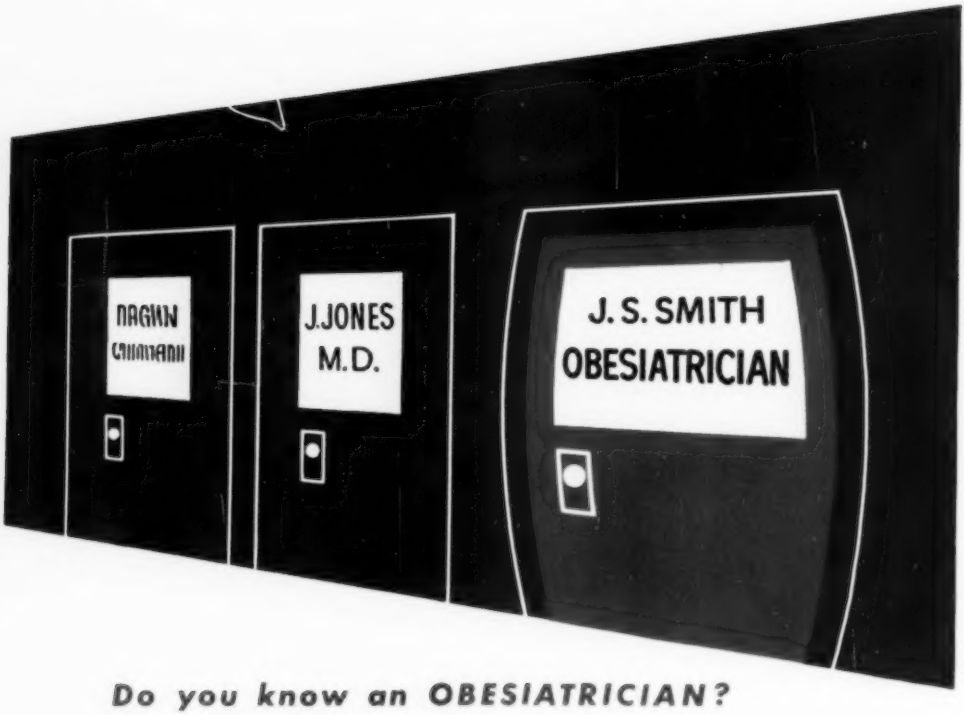
There are no real contraindications to the use of MEPHOSAL—no fear of serious toxic reactions—no fear of blood dyscrasias.

Please—*when prescribing specify the dosage form clearly.*

SAMPLES and literature on request. CROOKES LABORATORIES, INC. Crookes MINEOLA, N. Y.

Therapeutic Preparations for the Medical Profession

*Patent applied for



Do you know an OBESIATRICIAN?

It *could* be a full-time specialty—the treatment of obese patients. In fact, many physicians have reached the conclusion that it requires full-time application just to follow through on a single case; to reinforce the patient's will-power, sustain her (or his) mental equanimity, perhaps even stay her hand as it reaches out for that extra "little" piece of dessert.

No physician has that kind of time at his disposal.

But he can enlist the aid of clinically evaluated medication in support of his dietary instructions.

ADJUDETS supply dextro-amphetamine (as the well-tolerated phosphate) to depress appetite, yet keep the patient alert and in good mood. This easy-to-take candy-like form (only 15 calories per troche) makes taking it a welcome before-meals addition to an otherwise drab routine. ADJUDETS also supply multivitamins for diets that are restricted.

Wyeth
Philadelphia 2, Pa.

ADJUDETS®

D-AMPHETAMINE—MULTIVITAMIN TROCHES

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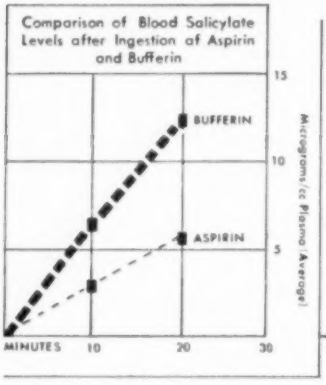
Medical Times is published monthly by Romaine Pierson Publishers, Inc., with publication offices at 34 North Crystal Street, East Stroudsburg, Pa. Executive, advertising and editorial offices at 676 Northern Boulevard, Great Neck, L. I., N. Y. Acceptance under section 34.64, P.L. and R., authorized February 23, 1950 at East Stroudsburg, Pa.

Faster Pain Relief with BUFFERIN®

1 ACTS TWICE AS FAST AS ASPIRIN

The antacids in Bufferin speed its pain-relieving ingredients through the stomach and into the blood stream. Actual chemical determinations show that within ten minutes after Bufferin is ingested blood salicylate levels are higher than those attained by aspirin in twice this time.[1]



2 DOES NOT UPSET THE STOMACH

Bufferin's antacid ingredients protect the stomach against aspirin irritation. This has been clinically demonstrated on hundreds of patients.

in usual doses

In a series of 238 cases, 22 had a history of gastric distress due to aspirin but only one reported any distress after taking 2 Bufferin tablets (equivalent to 10 grains of aspirin).[1]

in large doses

In a recent study group, 1006 patients received, over a 24 hour period, 12 Bufferin tablets (equivalent to 60 grains of aspirin). Although 72 had a history of being sensitive to aspirin, only 18 reported any gastric side-effect with Bufferin.[2]

1. Effect of Buffering Agents on Absorption of Acetylsalicylic Acid. J. Am. Pharm. Assoc., Sc. Ed. 39:21, Jan. 1950
2. Gastric Tolerance for Aspirin and Buffered Aspirin. Ind. Med. 20:480, Oct. 1951

INDICATIONS: Simple headaches, neuralgias, dysmenorrhea, muscular aches and pains, discomfort of colds and minor injuries. Particularly useful when gastric hyperacidity is a complication. Useful for relieving pain in the treatment of arthritis.

EACH BUFFERIN TABLET contains 5 grains of acetylsalicylic acid, together with optimum amounts of the antacids aluminum glycinate and magnesium carbonate.

AVAILABLE in vials of 12 and 36 tablets and in bottles of 100. Tablets scored for divided dosage.

Bristol-Myers Co., 19 West 50 St., New York 20, N. Y.

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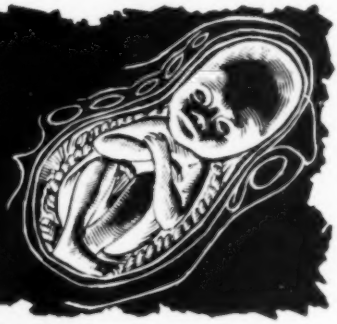
96% BIRTH RATE

with des or desPLEX



TWO DEPENDABLE PRODUCTS FOR LIFE *in* THREATENED ABORTION, HABITUAL ABORTION AND PREMATURE LABOR

des, the only micronized, triple crystallized (Grant Process) Stilbestrol (U.S.P.) Tablets—used in the treatment of pregnant women, with a history of one, two or more abortions—***averaged 96% normal live babies delivered***[1,2,3].

After extensive clinical experience with des, Karnaky[1], Gitman and Koplowitz[2] and Ross[3] as well as countless other clinicians wholeheartedly endorse the sound therapeutic necessity for the use of des in threatened abortion, habitual abortion and premature labor.

In a most recent publication, Karnaky has demonstrated that des, in massive doses (275 milligrams daily) provides optimum therapeutic results with maximum safety.

des—25 milligram tablets—highly micronized, triple crystallized (Grant Process) Stilbestrol (U.S.P.)—dissolve within a few seconds and are uniformly absorbed into the blood stream. Available in containers of 30 and 100 tablets.

new desPLEX—vitaminized, micronized Stilbestrol (U.S.P.). Border-line deficiency of B complex, especially Folic Acid, may sometimes prevent maximum utilization of estrogens. Histories of such cases indicate that the woman had difficulty in metabolizing endogenous or ingested estrogens. Not unusually, mild to severe nausea and vomiting is symptomatic. For additional support, when indicated, prescribe desPLEX, micronized Stilbestrol (U.S.P.), fortified with vitamin C plus B complex, including Folic Acid and B_{12}

Karnaky[4] and Javert[5] agree that C and B complex vitamins and Folic Acid are necessary for the normal physiological metabolism of estrogens. Jailer[6] further substantiates that a border-line deficiency of Folic Acid may result in premature separation of the placenta. *That is why desPLEX is the product of choice.*

desPLEX—25 milligram tablets—vitaminized, micronized, triple crystallized (Grant Process) Stilbestrol (U.S.P.) fortified with C and B complex vitamins, particularly Folic Acid. Available in containers of 30 and 100 tablets.

For further information, write:

Medical Director

GRANT CHEMICAL COMPANY, INC.

121 East 24th Street

New York 10, N. Y.

●

References:

1. Karnaky, K. J., Amer. J. Obst. & Gyn. 53:312, 1947. 2. Gitman, L. and Koplowitz, A., New York State J. Med. 50:2823, 1950. 3. Ross, J. S., N. Nat. M.A. 43:20, 1951. 4. Karnaky, Karl J., Surg., Gyn. & Obst. 91:617, 1950. 5. Javert, C. T., New York State J. Med. 48:2595, 1948. 6. Jailer, J. W., J. Clin. Endrocinol. 9:557, 1949.

Medical TIMES

THE JOURNAL OF GENERAL PRACTICE

Incorporating the Long Island Medical Journal and Western Medical Times

CONTRIBUTIONS Exclusive Publication: Articles are accepted for publication with the understanding that they are contributed solely to this publication, are of practical value to the general practitioner and do not contain references to drugs, synthetic or otherwise, except under the following conditions: 1. The chemical and not the trade name must be used, provided that no obscurity results and scientific purpose is not badly served. 2. The substance must not stand disapproved in the American Medical Association's annual publication, New and Nonofficial Remedies. When possible, two copies of manuscript should be submitted. Drawings or photographs are especially desired and the publishers will have half tones or line cuts made without expense to the authors. Reprints will be supplied authors below cost.

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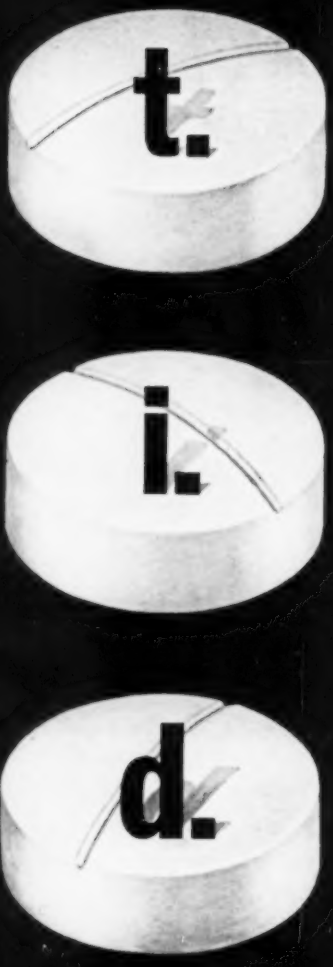
1st choice for oral penicillin therapy

just 1 or 2 tablets



Pentids

Squibb 200,000 Unit Penicillin G Potassium Tablets

SQUIBB

"PENTIDS" IS A TRADEMARK

BOARD OF ASSOCIATE EDITORS

a *penetrant* emulsion for chronic constipation

KONDREMUL® (PLAIN)

COLLOIDAL EMULSION OF MINERAL OIL AND IRISH MOSS

permeates the hard, stubborn stool of chronic constipation with millions of microscopic oil droplets, each encased in a film of Irish moss . . . makes it more movable

KONDREMUL *(Plain)*—Pleasant-tasting and non-habit-forming. Contains 55% mineral oil. Supplied in bottles of 1 pt.

KONDREMUL *(With Cascara)*—0.66 Gm. nonbitter Ext. Cascara per tablespoon. Bottles of 14 fl.oz.

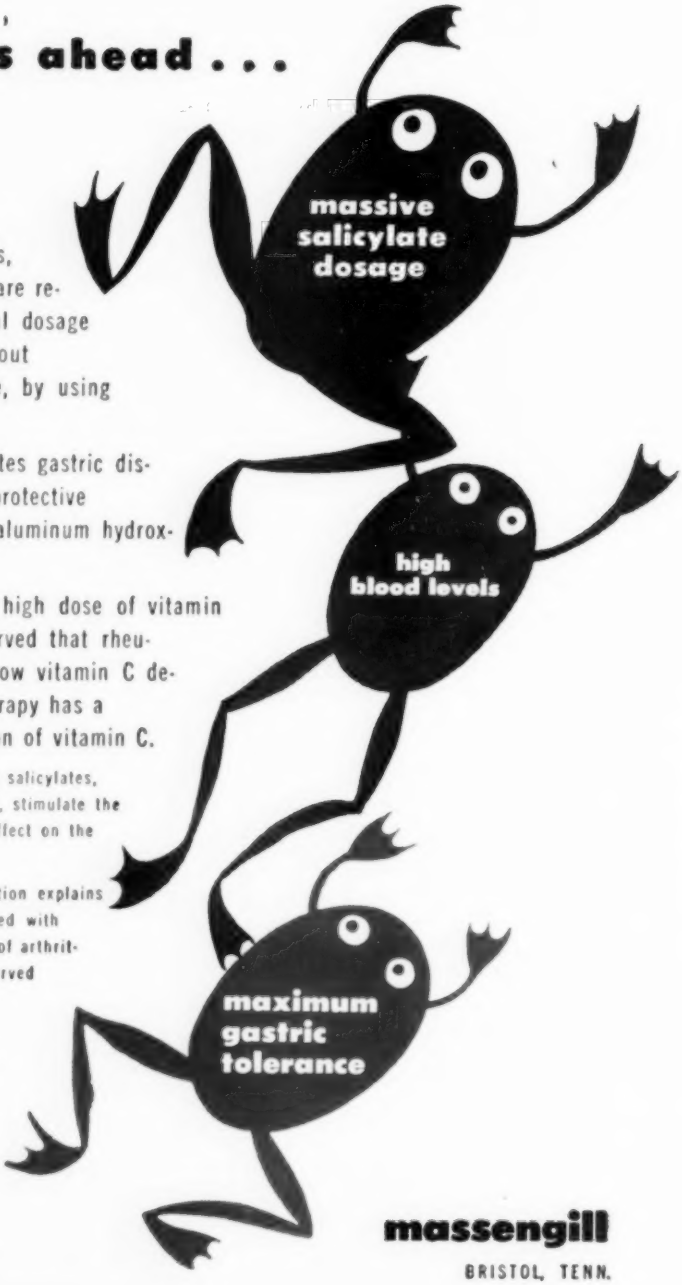
KONDREMUL *(With Phenolphthalein)*—0.13 Gm. phenolphthalein (2.2 gr.) per tablespoon. Bottles of 1 pt.

When taken as directed before retiring, KONDREMUL does not interfere with absorption of essential nutrients.

THE E. L. PATCH CO. — STONEHAM, MASSACHUSETTS

KONDREMUL PATCH

IN ARTHRITIS
three jumps ahead . . .



MASSIVE DOSAGE

To obtain maximum results, high salicylate blood levels are required. This means high oral dosage which can be attained, without excessive gastric disturbance, by using Salcedrox.

Salcedrox virtually eliminates gastric disturbance, because of the protective combination with activated aluminum hydroxide and calcium carbonate.

Salcedrox also contains a high dose of vitamin C, because it has been observed that rheumatic and arthritic states show vitamin C deficiencies, and salicylate therapy has a tendency to intensify depletion of vitamin C.

There is significant evidence that salicylates, through action on the hypothalamus, stimulate the pituitary, producing an ACTH-like effect on the adrenal cortex.*

This new concept of salicylate action explains many of the clinical results obtained with salicylate therapy in the treatment of arthritides and rheumatic afflictions—observed results that cannot be attributed to analgesic action alone.

*Proceedings Soc. Exp. Bio. Med., 1952, v80, 51-55, G. Cronheim, et al.

FORMULA

Sodium Salicylate .5 gr. (0.3 Gm.)
Aluminum Hydroxide Gel, dried ..... 2 gr. (0.12 Gm.)
Calcium Ascorbate ... 1 gr. (60 mg.) (equivalent to 50 mg. Ascorbic Acid)
Calcium Carbonate .1 gr. (60 mg.)

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BRISTOL, TENN.

send for professional literature

SALCEDROX

Off the Record . . .

True Stories From Our Readers

Each incident described has been contributed by one of our readers. Contributions describing actual and unusual happenings in your practice are welcome. For obvious reasons only your initials will be published. An imported German apothecary jar will be sent in appreciation for each accepted contribution.

Cum Laude

"Dr. Bernard Fantus who was one of the unique professors at Rush Medical College gave such philosophical and dramatic lectures, it was difficult to take notes, or outline. However, one of my friends who took the course before me recorded his lectures in shorthand. Being informed, I reluctantly would answer with a hesitating voice. At the end of a week the professor would say "Alright Mr. . . . what is the answer?" after other students failed to respond. At the end of the 6 weeks course I received a 98. Feeling guilty I went to his office to explain by unfair brilliance. When I arrived his nurse told me he expected me, which flustered me completely. As I went in I hemmed and hawed saying I was one of his students and that I took his course. He said he knew all that, and wondered what I wanted. So I explained what and how I did so well. His reply was that he had only one regret; could he have predicted my veracity; he would have given me 100 instead of 98.

S. E. L., M.D.
Beverly Hills, Calif.

Cheering Section

At St. Vincent's Hospital of this City, there was a very toxic thyroid case scheduled for an 8 a.m. thyroidectomy. Every effort had been taken to keep the patient quiet.

At 7:15 a.m. a group of about 20 honest, well-meaning folk were climbing the stairs to the 4th floor, their purpose quite clear. They were intercepted by a Sister, who asked them where they were going. They told her they were going to visit the lady who was going to be operated on that morning. Sister told them that she was going to have to be quiet before she went to the operating room.

The spokesman for the crowd assured her that they were well aware of that and that they were not all going in at one time, but that they were going into her room only 4 or 5 at a time and would not stay over 5 minutes. They just wanted to jolly her up a little before her operation. How do you think this story turned out? You are right, I was there watching and they were turned back.

C. B. J., M.D.
Birmingham, Ala.

Jet Propulsion

Dr. L. L. Hill, deceased of Montgomery, Alabama, used to have a good story about his first obstetrical case. The patient was in hard labor and one of the old ladies asked him, "Doctor, don't you think it is time to snuff her?" Dr. Hill replied, "Yes, I do," although he was uncertain as to what they had in mind.

The lady took a hollow tube, placed a wad of snuff in same and blew this into the patient's nostrils. She immediately sneezed and Dr. Hill said that he just barely caught the baby going over the foot of the bed!

G. G., M.D.
Birmingham, Ala.

—Concluded on page 21a

an important new

anticholinergic-antispasmodic agent

CENTRINE

TRADEMARK

Hydrogen Sulfate

Milligram for milligram, the most potent of all synthetic anticholinergic-antispasmodics available. Average dose is only ½ milligram *t.i.d.* or *q.i.d.*

Remarkably non-toxic. Incidence of side effects requiring temporary discontinuance of therapy has been reported as 1.5%.[1]

Available in solution for administration by the drop. Permits unlimited flexibility in titrating the dose to the individual patient in increments of 1/20 milligram.

Practically tasteless. No unpleasant immediate taste, no bitter after-taste, with either Centrine Tablets (uncoated) or Centrine Solution for drop-dosage.

Centrine is indicated in peptic ulcer, hypertrophic gastritis, pylorospasm, intestinal hypermotility, and related conditions in which spasmolytic and antisecretory effects are desired.

Supplied as scored tablets (uncoated), 0.5 mg., bottles of 100; and in solution, 0.05 mg. per drop, in 1 oz. bottles with dropper.

Bristol
LABORATORIES, INC.
SYRACUSE, NEW YORK

1. Bolt, R. J., Bratt, H., and Pollard, H. M., Gastroenterology 24: 204 (June) 1953

gentia·jel

ONLY gentian violet treatment you can prescribe

for

antibiotic moniliasis[1]

diabetic vulvitis[2]

vaginal thrush[3]

pregnancy moniliasis

93% clinically effective[4] in the most resistant cases during the last trimester of pregnancy

1. Editorial: J.A.M.A. 149:763 (June 21) 1952. 2. Bernstine, J.B. and Rakoff, A.D. "Vaginal Infections, Infestations, and Discharges," the Blakiston Co., Inc., 1953, p. 271. 3. Combined Textbook of Obstetrics and Gynecology, Edited by Dugald Baird, 5th Ed., E. & S. Livingstone Ltd., 1950. 4. Waters, E.G. and Wager, H.P.: American Jour. of Obstetrics & Gynecology, 60:885, 1950

AVAILABILITY: *gentia·jel* 12 single-dose plastic disposable applicators on prescription only.

SAMPLES ON REQUEST

Westwood Pharmaceuticals · 468 Dewitt Street, Buffalo 13, N.Y.

DIVISION OF FOSTER MILBURN CO.

Announcing

a new scientifically formulated product to control obesity

Revicaps*

REDUCING VITAMIN CAPSULES

d-Amphetamine-Vitamins and Minerals Lederle

reduces appetite . . . provides all essential diet factors . . . maintains morale

REVICAPS Reducing Vitamin Capsules is a new development of Lederle research, designed to provide a balanced appetite-depressant for the management of overweight patients.

The importance of weight-control in heart disease and other degenerative diseases cannot be over-emphasized. REVICAPS fills the double function of reducing appetite while providing all the essential vitamins and minerals listed in the formula at right.

d-Amphetamine sulfate—5 mg. per tablet—maintains morale, ends "diet irritability," keeps the patient on the diet and in good spirits.

Methylcellulose provides bulk.

The complete supply of vitamins and minerals eliminates the dangers of "starvation" diets.

Dosage: 1-2 capsules ½-1 hour before meals.

Each capsule contains:

d-Amphetamine Sulfate	5.00 mg.
Vitamin A	1670 U.S.P. Units
Vitamin D	167 U.S.P. Units
Thiamine HCl (B_1)	1.00 mg.
Riboflavin (B_2)	1.00 mg.
Niacinamide	20.00 mg.
Calcium Pantothenate	0.34 mg.
Pyridoxine HCl (B_6)	0.34 mg.
Folic Acid	0.34 mg.
Vitamin B_{12}	0.34 mcgm.
as present in concentrated extractives from streptomyces fermentation	
Ascorbic Acid (C)	20.00 mg.
Methylcellulose	200.00 mg.
Iron (FeSO exsiccated)	3.34 mg.
Calcium ($CaHPO_4$)	140.00 mg.
Phosphorus (CaHPO)	108.00 mg.
Iodine (KI)	0.50 mg.
Fluorine (CaF_2)	0.10 mg.
Copper (CuO)	1.00 mg.
Potassium (K_2SO_4)	5.00 mg.
Manganese (MnO_2)	1.00 mg.
Zinc (ZnO)	0.50 mg.
Magnesium (MgO)	1.00 mg.
Boron ($Na_2B_4O_7$)	0.10 mg.

*Trade-mark

Lederle

LEDERLE LABORATORIES DIVISION

AMERICAN Cyanamid COMPANY 30 Rockefeller Plaza, New York 20, N.Y.

—Concluded from page 17a

Cheap at Any Price

This patient came into my office yesterday and the conversation was as follows: "Doctor I want to know if I should get married. This man I knows wants to marry me. He went down last night and got the marriage license and I asked him if he could give me as much money as the pension I was getting. $50.46." He said, "No, he was buying a house and owed $300.00 more on it." I said, "Well we ain't going to get married." He said, "But Stella, I done bought the license and it cost me $4.75." "Here, take this $4.75, we ain't going to get married. Now doctor, don't you think I done right."

B. L. W., M.D.
Richmond, Va.

No Wonder

Recently I circumcised a husky, teenage, big boy, almost a young man. He had difficulty in voiding and the attendant said, "We will have to catheterize you." He was alarmed and greatly distressed, had his mother and others sent for, demanded their aid and intervention, "because," he told them, "I have just been informed that I am to be castrated!"

He was more alarmed because I had treated him for over a year for underdeveloped genitalia, with excellent results and here he was being stripped of his manhood in one foul stroke.

A happy ending was achieved upon explanation of the impending procedure.

S. A. L., M.D.
Birmingham, Ala.

So That's the Reason

A couple from the Ozarks had come in regularly each year to have a baby. Then the doctor noted that they had missed 3 to 4 years, and upon their arrival said, "How come you folk have not been down for several years?" The little Ozarkian said, "You know, Johnnie and I found out what caused this and now we are not having so much trouble."

* * *

I told this to a little girl in the hospital this morning who had been coming in regularly every year to have a baby. She said, "Well, we have been starting to get suspicious and now I am certainly going to tell my husband."

G. B. M., M.D.
Escondido, Calif.

Down To Earth

When I was on District Obstetrical Service as a Medical Student, I had a delivery in which several countrywomen, obviously midwives, invited themselves into "consultation" which consisted of an enthusiastic if garbled discussion of obstetrics. The high point in the discussion was reached when one inquired:

"Doctuh, Sir, What is this here *fungus* you doctors is always holding?"

W. R. H., M.D.
New York, N. Y.

King Size Medication

A few years ago I was treating a patient in the rural section. When he went to the drugstore for his medicine, he received another patient's medicine by mistake that was to be administered as a suppository.

My patient did not read the directions and in error, took one of the suppositories by mouth. When his next dose was due later at night, he did read the directions and, of course, found out his mistake, and the druggist's also.

Alarmed and panicky, he had his nephew drive him to my home in the small hours of the morning. When I sleepily assured him he would survive the ordeal, we both had a good laugh.

R. W. W., M.D.
Attalla, Ala.

Milk with a Blue Ribbon Pedigree

Here is another in a long line of famous Carnation champions bred and raised on the Carnation Farms. Cattle from these prize-winning bloodlines are shipped to local dairy farms throughout America to improve the quality of milk supplied Carnation processing plants.

Holder of World's Record for Butterfat Production

"From Contented Cows"

THE MILK EVERY DOCTOR KNOWS

Permapen®

Brand of dibenzylethylenediamine dipenicillin G

DBED

PENICILLIN

easy-to-give
easy-to-take
formulations

Pfizer

easy-to-give Permapen AQUEOUS SUSPENSION

As prophylactic therapy in rheumatic fever or in the adjunctive treatment of penicillin-sensitive infections, one intramuscular injection produces blood levels lasting as long as 14 days. *Easy-to-give* Permapen Aqueous Suspension is supplied in single-dose, disposable STERAJECT® cartridges containing 600,000 units of DBED penicillin. Each cartridge comes with sterile, individually wrapped needle, ready for immediate use in your Pfizer STERAJECT syringe.

long-lasting Permapen FORTIFIED AQUEOUS SUSPENSION

Embodies the higher blood levels produced by 300,000 units of procaine penicillin G crystalline and the protracted blood levels obtained from 300,000 units of DBED penicillin. Available in single-dose, disposable STERAJECT cartridges, each with its own sterile, individually wrapped needle.

easy-to-take Permapen ORAL SUSPENSION

Therapeutic benefits are independent of meals, and one teaspoonful—300,000 units of DBED penicillin—every 8 hours provides demonstrable blood levels 'round the clock in most patients. *Easy-to-take* Permapen Oral Suspension is peach-flavored, leaves no disagreeable after-taste. Supplied in 2 oz. bottles. No refrigeration needed.

Pfizer

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Division, Chas. Pfizer & Co., Inc.

routine . . .

for rapid control of bleeding

KOAGAMIN®

systemic aid to faster clotting

Because it acts directly on the clotting mechanism, KOAGAMIN — ACTS RAPIDLY — in minutes not hours.

ARRESTS ALL TYPES OF CAPILLARY AND VENOUS BLEEDING — (unlike vitamin K which is indicated only in relatively infrequent prothrombin deficiencies.)

IS SAFE — no untoward side effect, including thrombosis, has ever been reported.

Invaluable in everyday practice, KOAGAMIN is especially useful in *postpartum hemorrhage, uterine bleeding, prostatectomy, tonsillectomy, epistaxis, oral and nasal surgery, and gastric ulcer.*

KOAGAMIN, an aqueous solution of oxalic and malonic acids for parenteral use, is supplied in 10-cc. diaphragm-stoppered vials.

Chatham

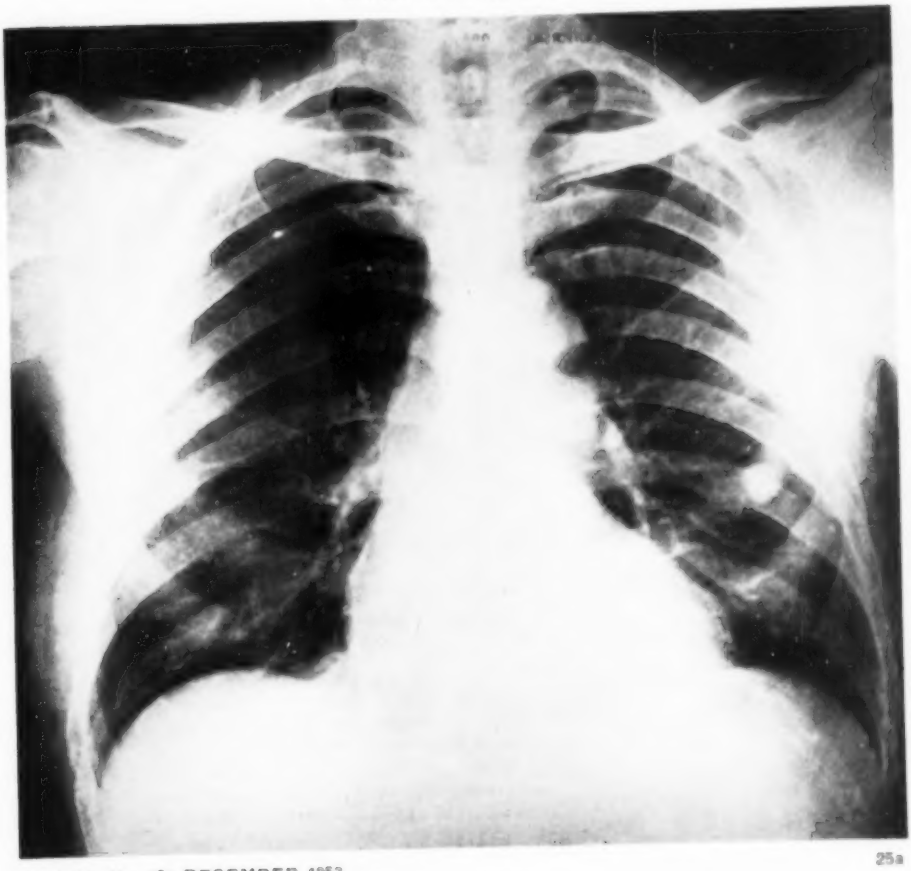
CHATHAM PHARMACEUTICALS, INC.
Newark 2, New Jersey

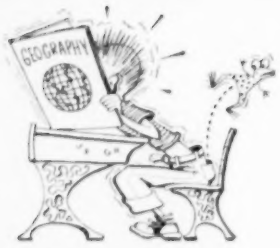
Diagnosis Please!

WHICH IS *YOUR* DIAGNOSIS?

1. Hamartoma
2. Metastatic malignancy
3. Tuberculoma
4. Early bronchogenic carcinoma
5. Adenoma

ANSWER ON PAGE 78A





You can't always tell a book by its cover

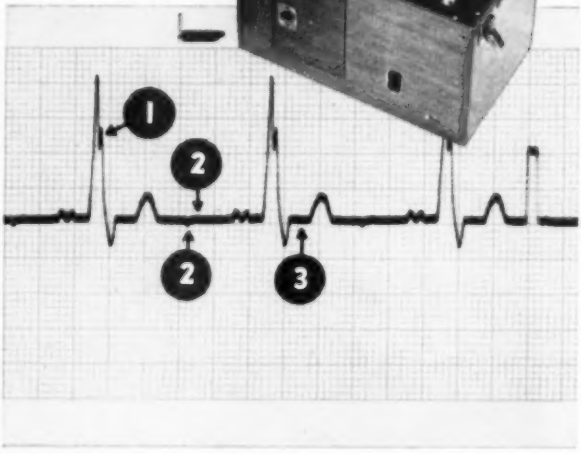
● The Viso-Cardiette's shipping carton is scientifically designed not only to provide safe transportation DIRECTLY to the user, but as the most convenient means for the instrument's RETURN to Sanborn Company, should it not be satisfactory after the no-obligation PRE-PURCHASE test.

But you can tell an electrocardiograph by its record

A test record is taken on each Viso-Cardiette, just prior to packing for shipment, as final proof of its performance. This is Sanborn Company's way of assuring the new owner that his instrument will record *accurately* the actual potentials encountered in clinical electrocardiography.

The record shown at right is a specimen of these proving tests. Not of physiological origin, the wave forms registered in this record were produced by an electronic device in order that a *selected variety* of voltage forms could be applied to the Viso, through its patient cable, and in this way show on one record that the instrument's characteristics will suit these wave forms.

Of special note in this record are conclusive proofs of the Viso's complete suitability, such as (1) the clearly registered notch in the R wave, showing response to *rapid* fluctuations, (2) the tiny positive and negative deviations in the baseline, showing that a pulse as small as 0.02 mv can be recorded clearly at normal sensitivity levels, the level base line, and the S-T segment (3) recorded on the isoelectric line *as it actually existed in the applied voltage.*



In addition to providing UNDISTORTED INFORMATION, Viso-Cardiette records have these advantages . . .

- They are in standard *rectangular coordinates*, which means no curvatures of complexes or time lines, or negative time intervals with which to contend.
- They may be standardized *during* leads, as well as before.
- Ordinarily, "AC" is eliminated *automatically* and *without* a ground wire by means of special circuits.
- The wide, ribbon-type baseline remains steady, even in locations where there is great fluctuation of line voltage.

Complete descriptive literature on the Viso-Cardiette, and details of an exclusive 15-day trial plan will be sent gladly on request.

Sanborn Company
CAMBRIDGE 39, MASSACHUSETTS

Upjohn

oral
estrogen-progesterone
effective in
menstrual disturbances:

Cyclogesterin
TRADEMARK, REG. U. S. PAT. OFF.
tablets

Each scored tablet contains:

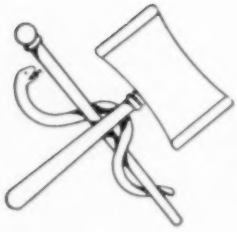
Estrogenic Substances* .. 1 mg.
(10,000 I.U.)

Progesterone .....30 mg.

**Naturally-occurring equine estrogens (consisting primarily of estrone, with small amounts of equilin and equilenin, and possible traces of estradiol) physiologically equivalent to 1 mg. of estrone.*

Available in bottles of 15 tablets.

The Upjohn Company, Kalamazoo, Michigan



What's Your Verdict?

Edited by Ann Picinich, Member of the Bar of New Jersey

In a game of high school basketball, the 17-year old daughter of the defendants, injured her foot. Within a few days it became exceedingly swollen and discolored. The parents, thinking the injury but a sprain, refused to provide any medical aid.

At the instance of an acquaintance, who fortuitously noticed the condition of her foot, the daughter visited a physician at his office. X-rays were taken, a fractured bone discovered, and the foot was set in a cast. The cast, and the use of crutches, must have been apparent to the parents with whom she resided. Had medical attention not been provided at the time, permanent injury would have resulted.

At the completion of his services, the physician rendered a bill for $45, to the parents, which they refused to pay on the ground that they did not authorize his services.

Is a parent obliged to pay the reasonable fee of a physician who renders necessary professional services to an infant child without the express or implied authority of the parent?

THIS COURT SAID: The duty of a parent to provide maintenance for his child was at common law a mere moral obligation; the parent was not legally compellable to perform this duty. The common law rule is now being discarded by this Court for a more equitable doctrine. Under this doctrine a parent is bound to provide his infant children with necessaries; and if he neglect to do so, a third person may supply them, and charge the parent with the amount. Normal instincts of humanity and plain common honesty as well as the substantial weight of judicial decisions in this country demonstrate the superiority of this equitable rule. Judgment was entered in favor of the physician plaintiff, for $45.

Decision of Supreme Court of New Jersey

"THIOSULFIL"®

brand of sulfamethylthiadiazole

The safest and most effective sulfonamide yet presented for urinary tract infections

provides these advantages...

Potent bacteriostatic activity

Rapid transport to site of infection for early and effective urinary concentration

Rapid renal clearance

Minimum toxicity

Minimum risk of sensitization

No alkalinization required

No forcing of fluids needed

GREATER SOLUBILITY + LOWER ACETYLATION = GREATER SAFETY

Now available in two dosage forms for greater convenience

SUSPENSION

No. 914—0.25 Gm. per 5 cc.
Bottles of 4 and 16 fluidounces

TABLETS

No. 785—0.25 Gm. per tablet
Bottles of 100 and 1,000

5340

Detailed literature giving complete dosage schedules is available to physicians.

AYERST, McKENNA & HARRISON LIMITED • New York, N. Y. • Montreal, Canada

In infectious and allergic rhinitis and sinusitis

Biomydrin "is effective as an antibiotic in clearing the nose of pathogenic organisms and purulent secretions. In many cases, sterile cultures were obtained after a brief period of treatment."

Antibiotics & Chemotherapy *3*:299 (March) 1953.

Improvement in 113 of 124 Patients*

Diagnosis	Number of patients	Improved
Chronic catarrhal rhinitis	11	11
Chronic allergic rhinitis	26	25
Right maxillary sinusitis	2	1
Chronic naso-pharyngeal catarrh	6	6
Chronic suppurative sinusitis	3	3
Coryza, Head cold, Catarrhal rhinitis	58	51
Influenza	2	1
Acute catarrh	4	3
Hypertrophic rhinitis	12	12
TOTAL	124	113 (91.1%)

* Eye, Ear, Nose and Throat Monthly *42*:512 (Sept.) 1953.

The Biomydrin formula

THONZONIUM BROMIDE 0.05%. Synthesized in the Nepera laboratories. Exceedingly potent antibacterial. Greatly enhances the antibiotic activity of neomycin and gramicidin. Reduces surface tension, facilitating spreading and penetrating. Mucolytic.

NEOMYCIN SULFATE 0.1%. Effective against gram-positive and gram-negative organisms.

GRAMICIDIN 0.005%. Effective against gram-positive organisms.

PHENYLEPHRINE HCl 0.25%. Widely preferred vasoconstrictor.

THONZYLAMINE HCl 1.0%. *Therapeutic concentration* of this effective antihistaminic aids in controlling local allergic manifestations.

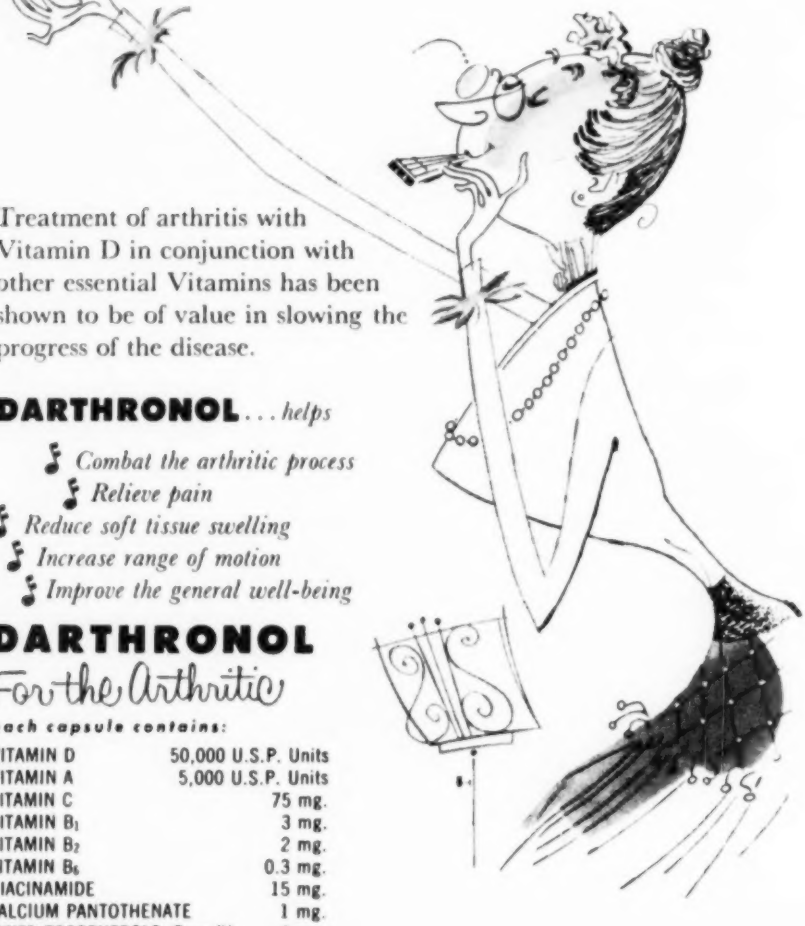
- Prompt, prolonged shrinkage of nasal mucosa without secondary congestion.
- pH is 6.2. Isotonic and buffered.
- Does not interfere with ciliary activity.
- Spray covers larger area than could be reached by drops.
- Available on prescription only.

DOSAGE: Adults—2 or 3 sprays in each nostril; 4 or 5 times a day as needed, or as directed by physician. Children—1 or 2 sprays in each nostril; 4 or 5 times a day as needed, or as directed by physician.

BIOMYDRIN

Nepera Chemical Co., Inc. Pharmaceutical Manufacturers, Yonkers 2, N. Y.

"D" is the key



Treatment of arthritis with Vitamin D in conjunction with other essential Vitamins has been shown to be of value in slowing the progress of the disease.

DARTHRONOL . . . *helps*

- *Combat the arthritic process*
- *Relieve pain*
- *Reduce soft tissue swelling*
- *Increase range of motion*
- *Improve the general well-being*

DARTHRONOL

For the Arthritic

each capsule contains:

VITAMIN D	50,000 U.S.P. Units
VITAMIN A	5,000 U.S.P. Units
VITAMIN C	75 mg.
VITAMIN B_1	3 mg.
VITAMIN B_2	2 mg.
VITAMIN B_6	0.3 mg.
NIACINAMIDE	15 mg.
CALCIUM PANTOTHENATE	1 mg.
MIXED TOCOPHEROLS (Type IV)	4 mg.

J. B. ROERIG AND COMPANY, CHICAGO 11, ILLINOIS

LETTERS TO THE EDITOR

This department is offered as an Open Forum for the discussion of topical medical issues. All letters must be signed. However, to protect the identify of writers, who are invited to comment on controversial subjects, names will be omitted when requested.

Straight Thinkers

Perhaps if you asked for a note of criticism from each of your readers you would be amazed at the response. I would bet that a large return mail would show most doctors in general practice like your journal best. MEDICAL TIMES has such expert selection of material for the average doctor, coupled with such clear writing for the busy doctor, the response would be no wonder. Personally I am inclined to believe that you and your editors are not only straight thinkers but old hands in private practice.

Sometimes I ask myself if doctors, in general, appreciate enough the services of our great drug houses. For my part I try to reciprocate by looking carefully at some of the advertising, and buying or prescribing some one or more of the products.

I wish to express my sincere thanks for MEDICAL TIMES with this note, a request that my address be changed.

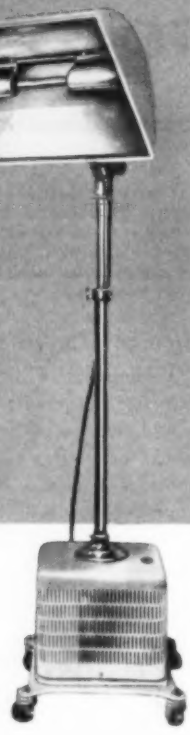
Homer A. Sweetman, M.D.
Baton Rouge, La.

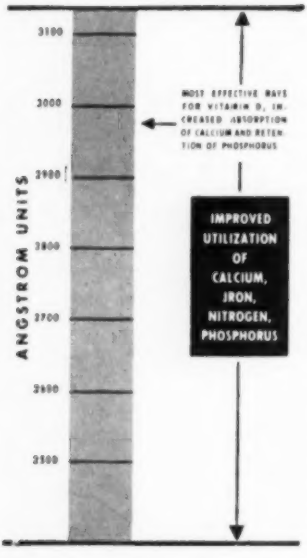
Keep Sending Refresher Reprints

In going over my copies of MEDICAL TIMES, I noticed the issues for January

—Concluded on page 55a

a prescription model lamp for home ultraviolet treatment





Hanovia Prescription Model Ultraviolet Lamp available on easy payment terms

Designed specifically for ultraviolet therapeutics in the patient's home, under the physician's supervision, this Hanovia Prescription Model Ultraviolet Quartz Lamp is a valuable aid to the physician. Such treatments permit patients who are unable to make repeated visits to the office to receive the benefits of ultraviolet with a maximum of convenience.

The ultraviolet emission of the prescription model lamp is in that part of the spectrum which is most effective for vitamin D production and for increased absorption of calcium and retention of phosphorus. In addition, these rays improve utilization of calcium, iron and nitrogen. The range is indicated in the accompanying chart.

Patients can purchase the Hanovia Prescription Model Ultraviolet Quartz Lamp from your regular surgical supply dealer, on convenient payment terms. Write for informative literature.

Hanovia Chemical & Mfg. Co., Dept. MT 1253
100 Chestnut Street, Newark 5, N. J.

HANOVIA

WORLD'S LARGEST PRODUCERS OF ULTRAVIOLET EQUIPMENT

Doctor, would it be helpful to you in your practice to know that there is a food available at reasonable prices in the stores the year round having these attributes:

1. One of the best "protective" foods with a well-rounded supply of vitamins and minerals.
2. Low sodium—very little fat—no cholesterol.
3. One of the first solid foods fed babies.
4. Useful in bland and low-residue diets.
5. Mildly laxative.
6. May be used in the management of both diarrhea and constipation.
7. Can be used in reducing diets.
8. Can be used in high-calorie diets.
9. Useful in the dietary management of celiac disease.
10. Useful in the dietary management of idiopathic non-tropical sprue.
11. Useful in the management of diabetic diets.
12. Valuable in many allergy diets.
13. A protein sparer.
14. Favorably influences mineral retention.
15. Useful in the management of ulcer diets.

FOR THE NAME OF THIS FOOD, PLEASE TURN THE PAGE

The answer is

B A N A N A S

If you would like

1. The authority for any of the statements made on the preceding page . . .

2. Additional information in connection with any of them . . .

3. The composition of the banana . . .

4. The nutritional story of the banana . . .

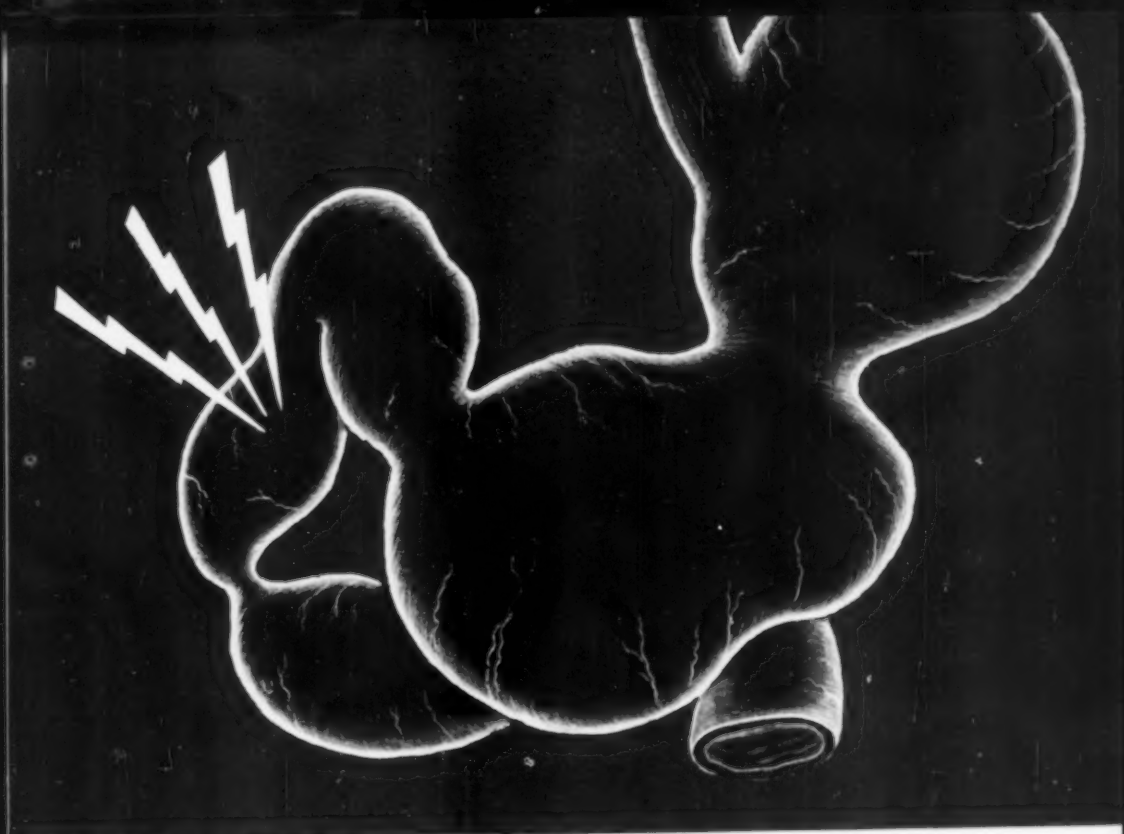
5. Information on various ways to prepare or serve bananas.

Please feel free to write to

Director, Chemical and Nutrition Research

United Fruit Company

PIER 3, NORTH RIVER, NEW YORK 6, N. Y.



Abnormal Motility as the Cause of Ulcer Pain

Until recently the general opinion was held that ulcer pain was primarily caused by the presence of hydrochloric acid on the surface of the ulcer.

Present investigations[1,2] on the relationship of acidity and muscular activity to ulcer pain have led to the following concept of its etiologic factor:

> "... abnormal motility[2] is the fundamental mechanism through which ulcer pain is produced. For the production and perception of ulcer pain there must be, one, a stimulus, HCl or others less well understood; two, an intact motor nerve supply to the stomach and duodenum; three, altered gastro-duodenal motility; and four, an intact sensory pathway to the cerebral cortex."

Clinical Application of Pro-Banthine®

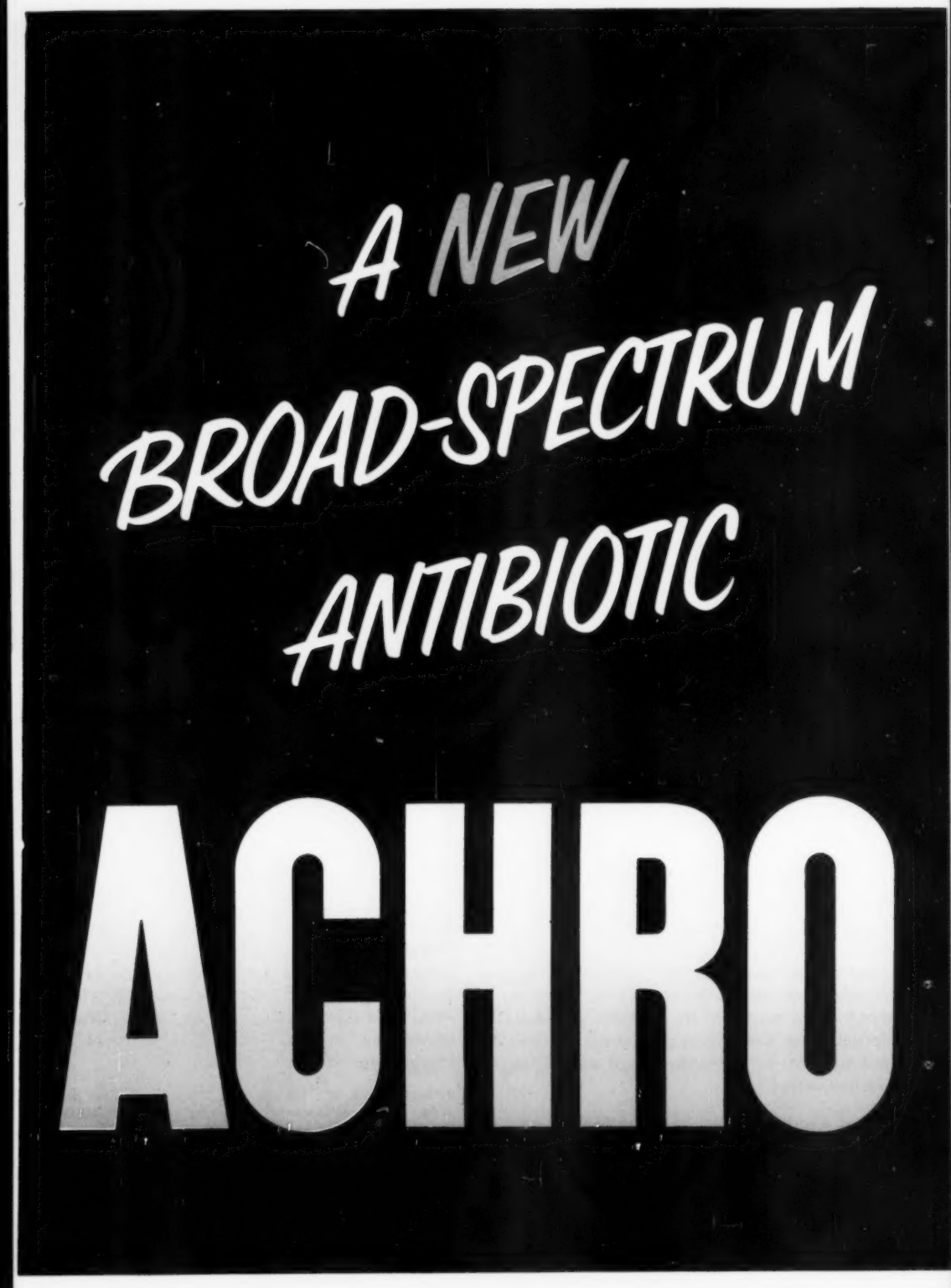
Pro-Banthine has been demonstrated consistently to reduce hypermotility of the stomach and intestinal tract and in most instances also to reduce gastric acidity. Dramatic remissions[1] in peptic ulcer have followed Pro-Banthine therapy. These remissions (or possible cures) were established not only on the basis of the disappearance of pain and increased subjective well-being but also on roentgenologic evidence.

Pro-Banthine (Beta-diisopropylaminoethyl xanthene-9-carboxylate methobromide, brand of propantheline bromide) has other fields of usefulness, particularly in those in which vagotonia or parasympathotonia is present. These conditions include hypermotility of the large and small bowel, hyperemesis gravidarum, certain forms of pylorospasm, pancreatitis and ureteral and bladder spasm.

1. Schwartz, I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthine, to be published.

2. Ruffin, J. M.; Baylin, G. J.; Legerton, C. W., Jr., and Texter, E. C., Jr.: Mechanism of Pain in Peptic Ulcer, Gastroenterology *23*:252 (Feb.) 1953.

SEARLE Research in the Service of Medicine


A NEW
BROAD-SPECTRUM
ANTIBIOTIC
ACHRO

More Rapid Absorption

Increased Toleration

Greater Stability

ACHROMYCIN, a new broad-spectrum antibiotic developed by the Lederle research team, has demonstrated greater effectiveness in clinical trials with the advantages of more rapid absorption, quicker diffusion in tissue and body fluids, and increased stability resulting in prolonged high blood levels.

ACHROMYCIN exhibits a broad range of activity against beta hemolytic streptococcic infections, *E. coli* infections (including urinary tract infections, peritonitis, abscesses), meningococcic, staphylococcic, pneumococcic and gonococcic infections, otitis media and mastoiditis, acute bronchitis and bronchiolitis, actinomycosis, mixed infections and many viral and rickettsial diseases.

ACHROMYCIN is now available in 250 mg., 100 mg., and 50 mg. capsules, SPERSOIDS® 50 mg. per teaspoonful (3.0 Gm.), Intravenous 500 mg., 250 mg. and 100 mg. Other dose forms will become available as rapidly as research permits.

Lederle

LEDERLE LABORATORIES DIVISION

AMERICAN Cyanamid COMPANY

30 Rockefeller Plaza, New York 20, N.Y.

MYCIN®

TETRACYCLINE CAPSULES LEDERLE

In all types OF DIARRHEA

Arobon®

(POWDERED CAROB FLOUR)

Fast, Positive Relief

Employed as the sole medication, Arobon quickly controls the simple diarrheas so frequently encountered in patients of all ages. Prepared from specially processed carob flour, it provides a high natural content of pectin, lignin, and hemicellulose. Its water-binding action promptly leads to formed stools, and the occluding activity of its contained pectin and other complex carbohydrates binds and removes offending toxins and bacteria. Arobon is pleasant to take and tends to counteract the nausea associated with diarrhea.

No Interference with Antibiotic Absorption

Clinical studies have shown that Arobon does not interfere with the absorption of orally administered broad spectrum antibiotics. Hence it can be given to advantage in the specific dysenteries in conjunction with antibiotic therapy for its valuable action upon intestinal motility.

The average single dose for adults is 2 tablespoonfuls in 4 oz. of milk, and for children, 1 tablespoonful in 4 oz. of milk, for infants, 2 teaspoonfuls in 4 oz. of water or skim milk and boiled for ½ minute.

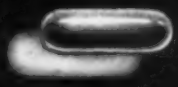
Arobon is available in 5 oz. bottles at all pharmacies.

THE NESTLÉ COMPANY, INC.

WHITE PLAINS, NEW YORK

especially for the carriage trade...

Children like Vi-Penta Drops because they taste good. Mothers like them because they are easy to give in milk, fruit juice, formula or dropped directly on the tongue. Doctors like them because they provide required amounts of vitamins A, C, D, and important B-complex factors, and because they're dated to insure full potency. Vi-Penta® Drops 'Roche' in packages of 15, 30 and 60 cc with calibrated dropper.



new higher potency

DORMISON 500 mg.

for restful sleep

"...because of its

absence of after-effects."

Malone, H. J.; Klimkiewicz, G. R., and Gribetz, H. J.: A Study of the Hypnotic Effect of Dormison in Children, J. Pediat. 41:153, 1952.

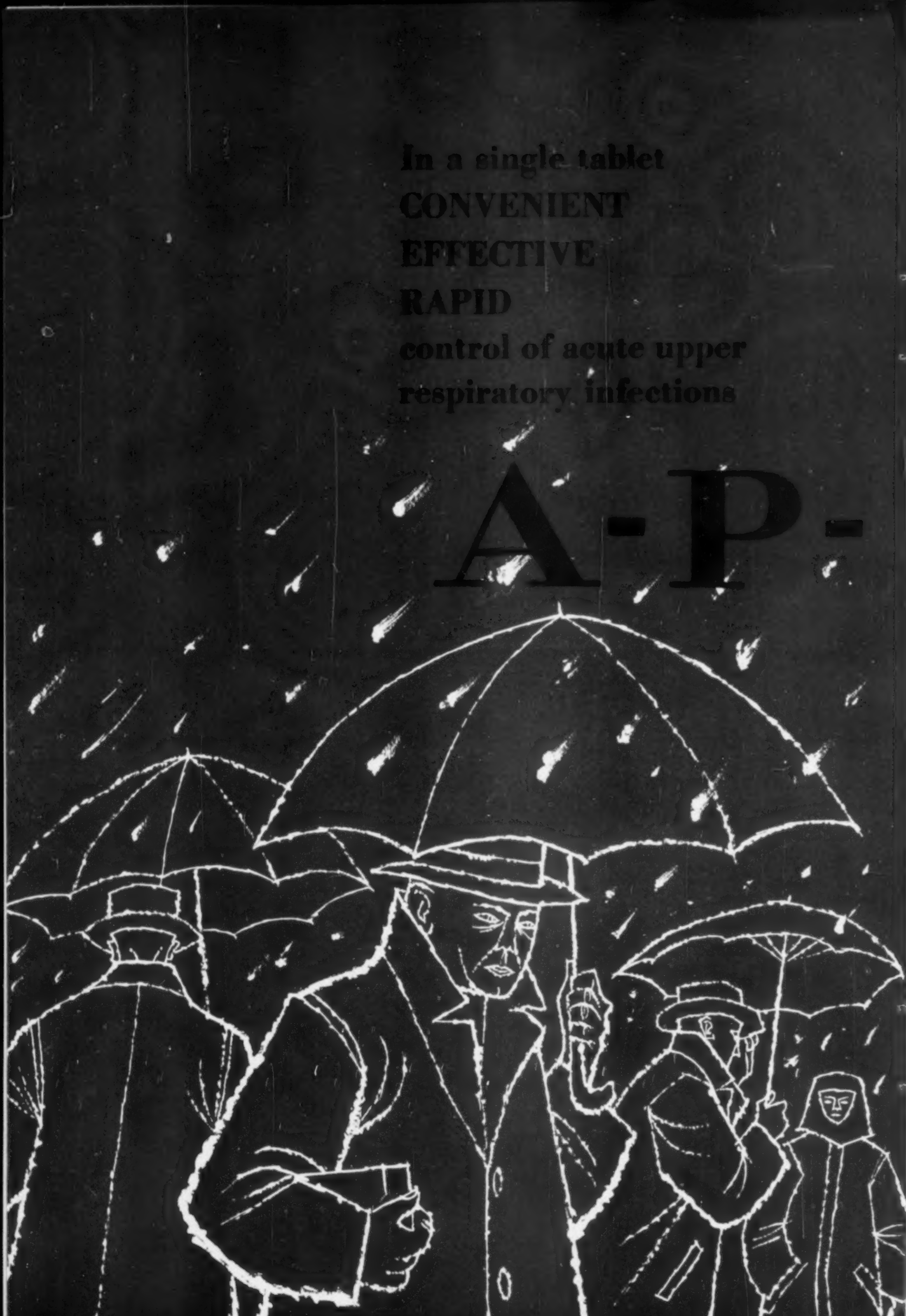
"...may be regarded as probably

the hypnotic of choice."

May, P. R.A., and Ebaugh, F. G.: Use of Hypnotics in Aging and Senile Patients: A Clinical Study of Dormison, J.A.M.A. 152:801, 1953.

DORMISON,® brand of methylparafynol, is available *only on prescription.* Do not confuse it with any product advertised to the laity.

DORMISON 500 mg.


In a single tablet
CONVENIENT
EFFECTIVE
RAPID
control of acute upper
respiratory infections
A-P-

Finke[1], urging a more extensive use of penicillin "at an early stage of respiratory infection," states: "Nearly all minor upper respiratory infections may be precursors of more severe conditions, especially in persons with previous major respiratory episodes. Therefore, the use of antibacterial agents in the treatment of bronchitis and similar illnesses has been justly advocated as a rational measure..."

CILLIN

Each A-P-Cillin tablet combines the following proved therapeutic agents:

1 • APC—for analgesic and antipyretic action—to relieve systemic symptoms.

Acetylsalicylic acid	2½ gr.
Phenacetin	2 gr.
Caffeine	½ gr.

2 • ANTIHISTAMINE—for local symptomatic relief, particularly from profuse nasal discharge, and for mild sedation.

Phenyltoloxamine dihydrogen citrate	25 mg.

3 • PENICILLIN—for prevention and control of secondary bacterial infections.

Procaine penicillin G	100,000 units

For the common acute upper respiratory infections, the usual adult dose is 2 tablets three times a day, best continued for at least three days. The tablets should be taken at least one hour before meals or two hours after meals.
White Laboratories, Inc., Kenilworth, N. J.

—supplied in bottles of 50 and 500 tablets.

1. Finke, W.: A.M.A. J. Dis. Child. 83:755, 1952.

You seldom see one . . .

without the other

Since anemia is usually accompanied by nutritional deficiencies, an effective hematinic should furnish adequate amounts of the Vitamins, Minerals and Trace Elements needed for optimum nutrition as well as those essentially concerned with hemopoiesis.

Clinicians have found that a striking clinical and hematologic response characterized by a marked increase in strength, vigor and appetite follows the administration of HEPTUNA PLUS.

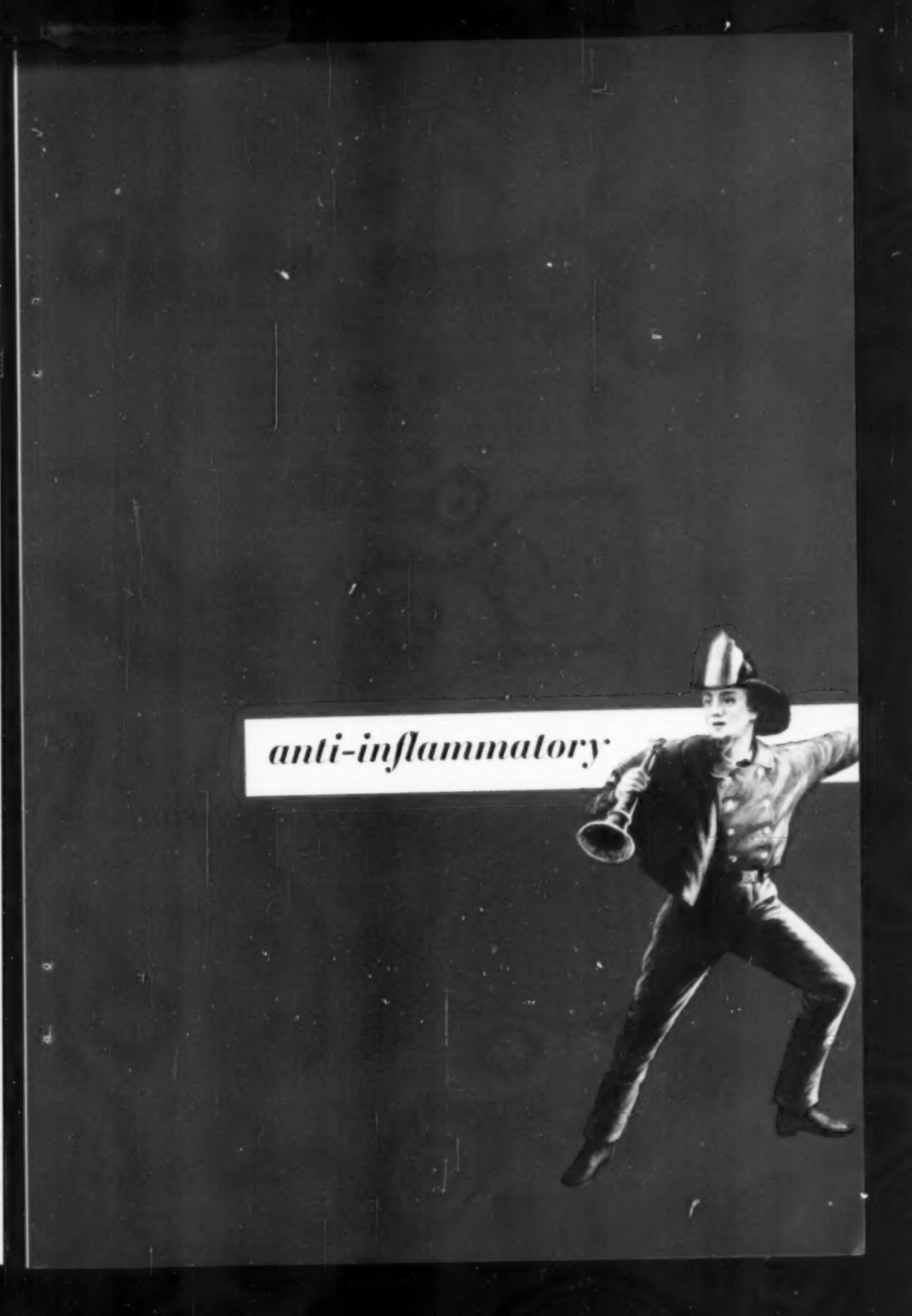
Specify **Heptuna plus**

Each capsule contains:

Ferrous Sulfate U.S.P.	4.5 gr.
Vitamin B_{12}	5.0 mcg.
Folic Acid	0.33 mg.
Ascorbic Acid	50.0 mg.
Vitamin A	5,000 U.S.P. units
Vitamin D	500 U.S.P. units
Thiamine Hydrochloride	2 mg.
Riboflavin	2 mg.
Pyridoxine Hydrochloride	0.1 mg.
Niacinamide	10 mg.
Calcium Pantothenate	0.33 mg.
Cobalt	0.1 mg.
Copper	1 mg.
Molybdenum	0.2 mg.
Calcium	37.4 mg.
Iodine	0.05 mg.
Manganese	0.033 mg.
Magnesium	2 mg.
Phosphorus	29.0 mg.
Potassium	1.7 mg.
Zinc	0.4 mg.

With other B-Complex Factors from Liver

J. B. ROERIG AND COMPANY, CHICAGO 11, ILLINOIS


anti-inflammatory

Today **Cortril**

brand of hydrocortisone

CORTRIL ACETATE TOPICAL OINTMENT
in 1/6-ounce tubes in two strengths — 1.0% and 2.5%

CORTRIL ACETATE OPHTHALMIC OINTMENT
in 1/8-ounce tubes in two strengths — 0.5% and 2.5%

CORTRIL ACETATE AQUEOUS SUSPENSION
for intra-articular injection in 5-cc. vials, 25 mg. per cc.

PFIZER SYNTEX PRODUCTS

PFIZER LABORATORIES, *Brooklyn 6, New York*
Division, Chas. Pfizer & Co., Inc.

Pfizer

A notable advance

In this decade of medical history marked by brilliant progress in antibiotic therapy and hormonal research, a notable advance in anti-inflammatory therapy has been achieved through collaborative steroid research by the Pfizer and Syntex organizations.

With the introduction of CORTRIL Topical Ointment, CORTRIL Ophthalmic Ointment, and CORTRIL Aqueous Suspension, significant and definite local anti-inflammatory action is now possible *without systemic effects.*

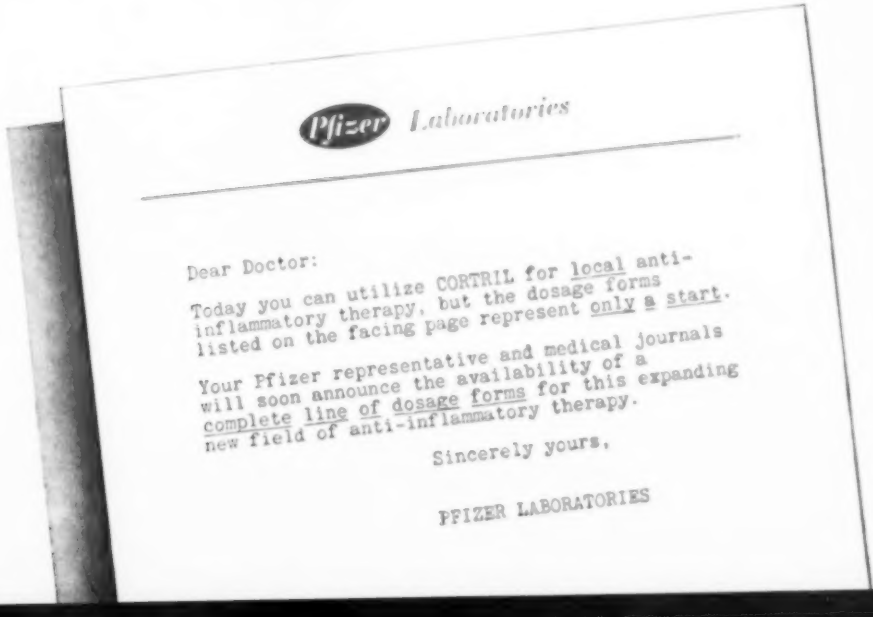
In a wide variety of dermatoses, CORTRIL Topical Ointment rapidly relieves pruritus, local edema, erythema, and inflammatory infiltration.

In external ocular disorders, CORTRIL Ophthalmic Ointment safely reduces local inflammatory edema and significantly inhibits fibrous tissue proliferation and corneal vascularization which can result in scarring.

In inflamed joints, sprains, and bursitis, CORTRIL Aqueous Suspension provides marked decrease in pain, stiffness, and swelling, entirely through local action.

The concurrent use of CORTRIL and TERRAMYCIN provides both anti-inflammatory and anti-infectious therapy — desirable as well as a useful precaution in many indications.

the anti-inflammatory hormone



Pfizer *Laboratories*

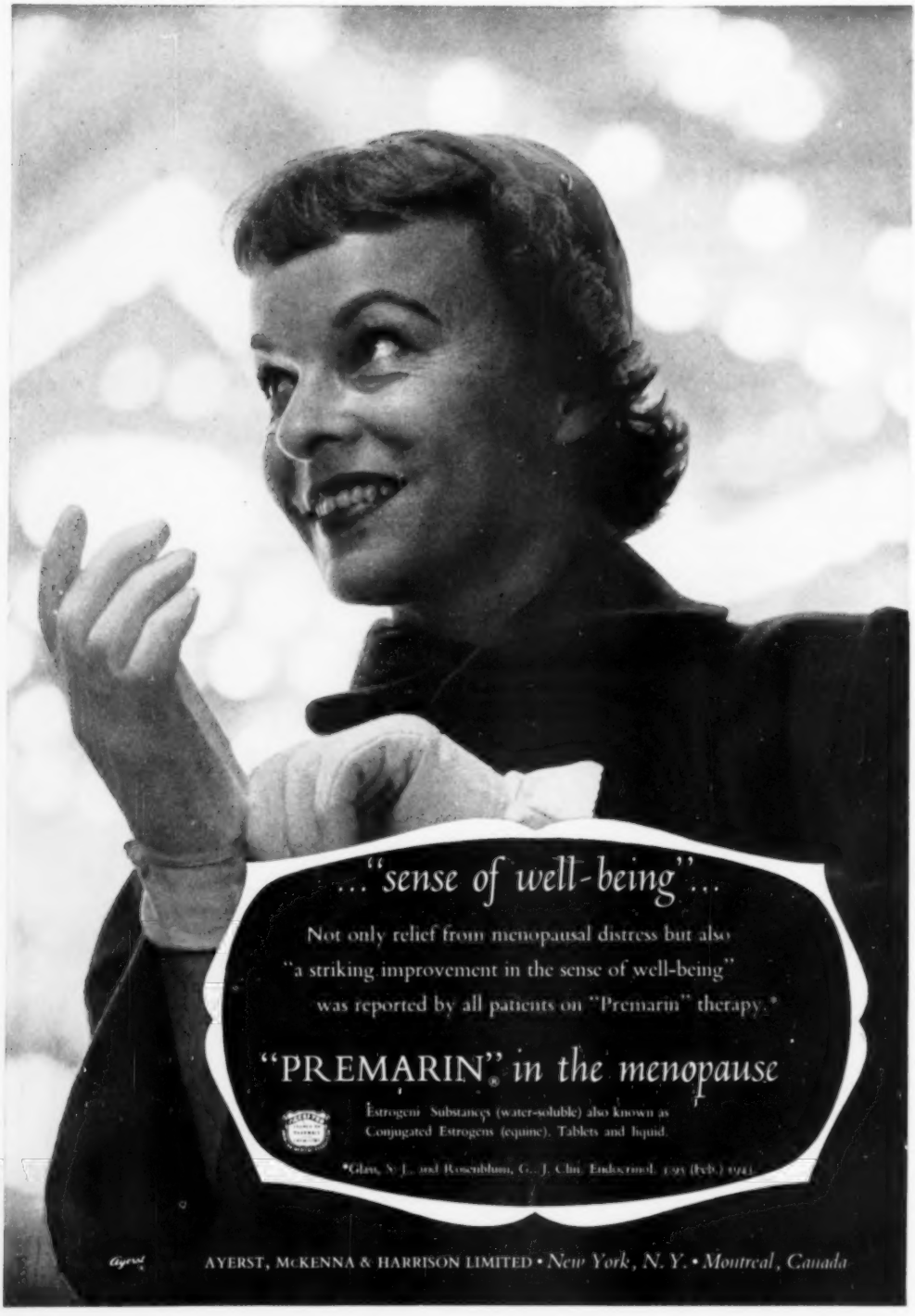
Dear Doctor:

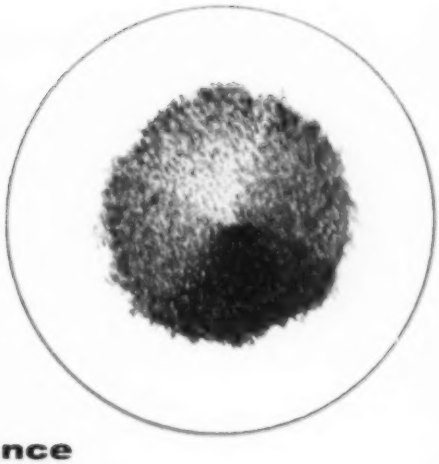
Today you can utilize CORTRIL for local anti-inflammatory therapy, but the dosage forms listed on the facing page represent only a start.

Your Pfizer representative and medical journals will soon announce the availability of a complete line of dosage forms for this expanding new field of anti-inflammatory therapy.

Sincerely yours,

PFIZER LABORATORIES


...“sense of well-being”...
Not only relief from menopausal distress but also
“a striking improvement in the sense of well-being”
was reported by all patients on “Premarin” therapy.*
“PREMARIN”® in the menopause
Estrogenic Substances (water-soluble) also known as
Conjugated Estrogens (equine). Tablets and liquid.
*Glass, S. J., and Rosenblum, G., J. Clin. Endocrinol. 3:93 (Feb.) 1943.
Ayerst
AYERST, McKENNA & HARRISON LIMITED • New York, N. Y. • Montreal, Canada



for restoration

and maintenance

of normal bowel function

Siblin

BULK-LUBRICANT FOR PHYSIOLOGIC TREATMENT OF CONSTIPATION

SIBLIN provides a granular, water-absorbent derivative of plantago which mixes intimately with food residues to form a soft, gelatinous mass in the large intestine. Nonirritating and virtually unaffected by digestive ferments, this smooth, cohesive mass provides bulk and lubrication for easy passage through the bowel. To aid in improving peristaltic function, SIBLIN contains, in each heaping teaspoonful, approximately 2 mg. of vitamin B_1.

In systematic treatment for chronic constipation, regular ingestion of SIBLIN encourages re-establishment of normal bowel function. In diarrhea, SIBLIN promotes the formation of stools of normal consistency, and following hemorrhoidectomy it helps assure soft stools.

Dosage: constipation, two teaspoonfuls, morning and night, with a full glass of water.
diarrhea, three heaping teaspoonfuls, or more, with a full glass of water, as required.
hemorrhoidectomy, one teaspoonful with a full glass of water, after meals.
supplied: 4-ounce and 16-ounce packages.

MEDICAMENTA PARKE DAVIS

Parke, Davis + Company

A *Leeming* First:

the **New** *coronary vasodilator*

Metamine®

Leeming brand of triethanolamine trinitrate biphosphate

more effective in angina prevention

than other coronary dilators. When taken routinely, METAMINE prevents anginal attacks or greatly diminishes their number and severity. In addition, METAMINE is apparently nontoxic, even in prolonged or excessive dosage.

there is a reason

METAMINE is chemically distinct from all other organic nitrates in that it has a nitrogen, rather than a carbon linkage. This perhaps explains its greater effectiveness and freedom from side effects.

Dosage: METAMINE is effective in a dosage of **only 2 mg.** To prevent anginal attacks, swallow 1 METAMINE tablet after each meal, and 1 or 2 tablets at bedtime. Full preventive effect is usually attained after third day of treatment.

Supplied: METAMINE tablets, **2 mg.**, vials of 50.

Thos. Leeming & Co. Inc. 155 EAST 44TH STREET, NEW YORK 17, N.Y.

CORICIDIN

controls colds... curbs complications

...complicated colds

New CORICIDIN with Penicillin G PROCAINE 150,000 units

combats secondary invaders
antibiotic + antihistaminic, analgesic, antipyretic

...simple colds

CORICIDIN

most widely prescribed preparation for prevention and treatment of symptoms

...and for pain

CORICIDIN with Codeine* ¼ or ½ gr.

valuable in sinusitis, headache, myalgia, neuralgia, pleurisy, bursitis, grippe

*Subject to Federal Narcotic Regulations.

Each CORICIDIN® Tablet contains CHLOR-*TRIMETON*® Maleate, aspirin, acetophenetidin, and caffeine.

Schering

CORICIDIN

Q.S.

is now possible

FOR LARGE DOSAGE OF ASPIRIN...

THE FIRST CLINICALLY PROVEN ENTERIC-COATED ASPIRIN

ASTERIC Brewer

ASTERIC Brewer (5 gr. enteric-coated Aspirin) ***Allows Greater Dosages***— 40, 50, 60, 70 or more grains daily as required where gastric distress and other irritating symptoms resulting from high dosages of plain aspirin tablets are contraindicated.

ASTERIC Brewer is indicated in the treatment of certain rheumatic disorders requiring maximal dosage of aspirin over long periods. *"Enteric-coated aspirin (ASTERIC) has an analgesic effect equal to that of regular aspirin and the onset of its action is only slightly delayed."* Clinically it was shown that equal blood levels were obtained.*

ASTERIC Brewer (5 gr. enteric-coated Aspirin) will be found beneficial for those patients suffering from hemorrhagic gastritis resulting from the irritating effects of plain aspirin and for cases of peptic ulcer which require acetylsalicylic acid therapy.

ASTERIC Brewer (5 gr. enteric-coated marbleized tablets) supplied in bottles of 100 and 1000.

FOR SAMPLES—just send your ℞ *blank marked 11AS12*

*Talkov, R. H., Ropes, M. W., and Bauer, W.: *The Value of Enteric Coated Aspirin.* N.E.J. Med. 242.19 (Jan. 5) 1950.

Brewer EST. 1852

BREWER & COMPANY, INC.

WORCESTER 8, MASSACHUSETTS U.S.A.

...she's the picture of misery, doctor, whenever she catches cold...

a simpler, safer way to relieve "STUFFED-UP NOSE"

What mother . . . when her youngster has a "stuffed-up nose" . . . remembers your warnings about indiscriminate use of topical applications?

Novahistine, *taken orally*, reduces nasal congestion promptly. It eliminates *your* problem of "overtreatment" between office visits . . . and *mother's* problem of administering drops or sprays to a rebellious child.

The vasoconstrictor agent(1) in Novahistine causes no cerebral excitement and does not lose effectiveness with repeated dosage. Its action is potentiated by one of the most effective, least toxic histamine antagonists.(2)

NOVAHISTINE IS AVAILABLE AS A PALATABLE ELIXIR AND SMALL, EASY-TO-TAKE TABLETS.

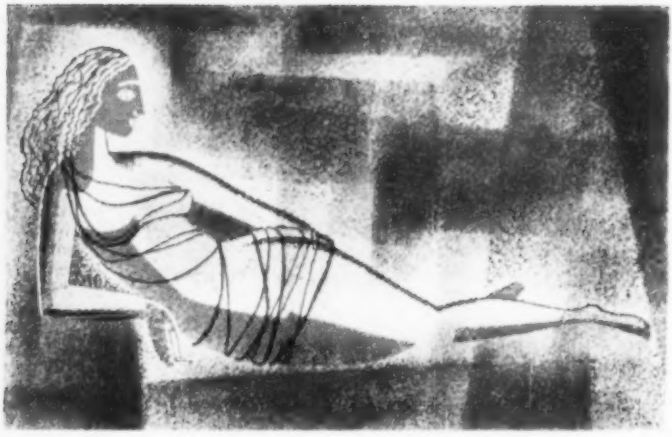
NASAL DECONGESTION . . . WITH ORAL DOSAGE

NOVAHISTINE*

Each teaspoonful or tablet provides:
(1) Phenylephrine hydrochloride..... 5.0 mg.
(2) Prophenpyridamine maleate.... 13.5 mg.

PITMAN-MOORE COMPANY
Division of Allied Laboratories, Inc., Indianapolis, Ind.

*TRADEMARK



a new oral antimenorrhagic

BLUTENE

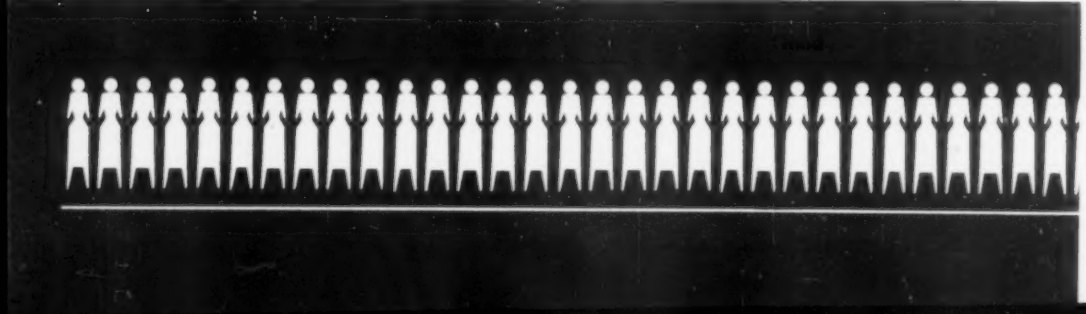
TRADE MARK

CHLORIDE

(TOLONIUM CHLORIDE, ABBOTT)

In a clinical study[1] of 63 hypermenorrhea cases, Blutene

helped 60 patients out of 63



IN CLINICAL TESTS, Lathrop and Carlisle[1] treated 63 women for hypermenorrhea, using the new BLUTENE therapy. Dosage was oral, at home. Each patient took one 100-mg. tablet of BLUTENE after meals, 3 times daily, for the duration of bleeding.

Results were noteworthy: 45 patients reported "good" results, 15 "fair," 3 "poor." Only 2 patients in the "good" group had recurrences. The authors conclude the treatment to be effective in selected patients.*

***IMPORTANT:** *BLUTENE should be used only after adequate gynecologic examination has ruled out organic disease as the cause of bleeding.*

A NEW IDEA

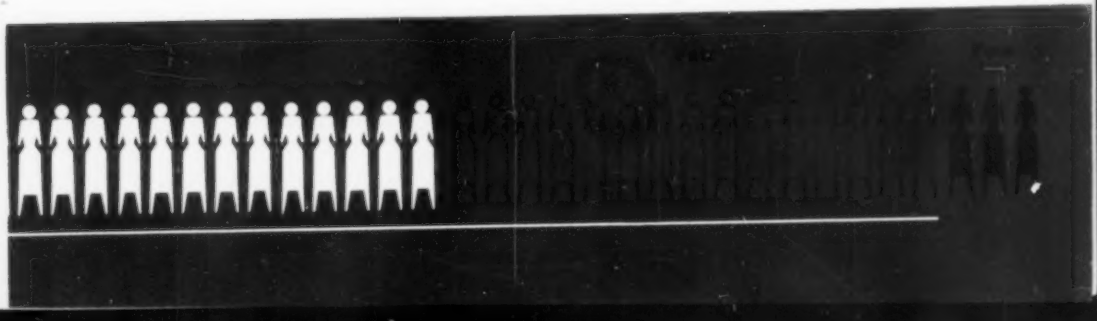
BLUTENE is a new concept in menotherapy. The drug bears no structural resemblance to any existing antimenorrhagic. It is nonhormonal.

It neutralizes excess heparin-like substances, often to end symptoms within one course of treatment[2] (although long-standing cases may require longer treatment). Side effects are usually minor[1,2,3,4] and often absent. If tenesmus or burning on urination occur, these side effects are ordinarily relieved by increasing the patient's fluid intake; if persistent nausea is encountered, smaller dosage may be better tolerated and still prove effective.

BLUTENE has been effective in some cases where estrogens, thyroid extract, curettage, etc. have failed.[2]

Provided in sugar-coated, brown, 100-mg. tablets, bottles of 25 and 100.
WRITE TODAY for complete descriptive literature.
Abbott Laboratories, North Chicago, Illinois. Abbott

1. Lathrop, C. A., and Carlisle, W. T., Oral Toludine Blue in the Treatment of Hypermenorrhea, Amer. J. Obst. & Gynec., 64:1376, December, 1952. **2.** Rumbolz, W. L., Moon, C. F., and Novelli, J. C., Use of Protamine Sulfate and Toludine Blue for Abnormal Uterine Bleeding, Amer. J. Obst. & Gynec., 63:1029, May, 1952. **3.** Priddle, Harold, Discussion of Rumbolz et al., Amer. J. Obst. & Gynec., 63:1036, May, 1952. **4.** Bickers, W., Toludine Blue—An Evaluation in the Treatment of Uterine Bleeding, in press, Amer. J. Obst. & Gynec.



Even a few pounds overweight can be dangerous

Statistics prove that marginal overweight—overweight of only 5% to 14%—increases mortality by 22%. Marginal overweight means, for example, an excess of only eight pounds in a patient whose ideal is 150.

'Dexedrine' Sulfate—with marginal overweight as with gross obesity—is the agent of choice for control of appetite in weight reduction.

Smith, Kline & French Laboratories, Philadelphia

Dexedrine* Sulfate Tablets • Elixir • Spansule† capsules

Standard in weight reduction

*T.M. Reg. U.S. Pat. Off. for dextro-amphetamine sulfate, S.K.F. †Trademark for S.K.F.'s brand of sustained release capsules (patent applied for).

LETTERS TO THE EDITOR

—Concluded from page 33a

1953 and May 1953 are missing. Diligent search of my home and office has not revealed them, and I would like to procure these missing issues if at all possible.

As a further favor, may I have any copies you have on hand of the refresher articles. This response is made in reference to your offers in various issues of MEDICAL TIMES.

I fail to see where any good purpose is being served by an increasing research into finer and finer divisions of the already dense jungle of analytical knowledge. Your publication comes along to the G.P. who struggles every minute of his day to derive some plausible synthesis of modern medical knowledge, as a log drifts downstream to a drowning man. Keep sending the refreshers!

John T. Anderson, M.D.
Minneapolis, Minn.

Refreshers Satisfying

I received the reprint I requested and want to thank you very much.

Such summaries satisfy a G.P.'s need for a comprehensive and practical understanding of a subject, so necessary in medical practice.

I consider all of these refresher articles extremely useful.

R.S., M.D.
Fort Worth, Texas

Corrigendum

On page 41a of the November issue the last paragraph of Dr. Griffith's letter should have read as follows:

6. The technic of lid suture illustrated in the small schematic drawings admittedly might result in notching of the lid in some instances. This possibility can be prevented by producing a lap-joint, as illustrated in the accompanying drawings below. A layer of fine silk sutures in the tarsal plate, however, is not objectionable.

the first
compound
effective against
motion sickness
in a single
daily dose

Pfizer

with just **4** *tablets*

of new **BONAMINE**

you can travel from . . .

Boston to Bangkok—*a 2 day trip*

. . . with new freedom from airsickness

MOST PROLONGED ACTION

Bonamine is the only motion-sickness preventive which is effective in a *single daily dose*. Just two 25 mg. tablets (50 mg.) will provide adequate protection against all types of motion sickness — car or boat, train or plane — for a *full 24 hours in most persons.*

new Bonamine*

BRAND OF PARACHLORAMINE HCl

FEW SIDE EFFECTS

Clinical studies have shown, in case after case, that relatively few of the patients experienced the usual side effects observed with other motion-sickness remedies: less drowsiness, dullness, headache, dryness of the mouth, etc.

Supplied: 25 mg. tablets, bottles of 100.

PFIZER LABORATORIES *Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.*

*TRADEMARK

11 reasons to consider MANDELAMINE in urinary infections

1 Controls most common urinary infections in 3 to 14 days.[1,2,3]

2 Bacteriostatic and bactericidal action is of approximately the same order as sulfonamides or streptomycin.[4,5,6,7] Effective against gram-positive and gram-negative organisms.

3 Bacteria do not develop resistance.[5,8,9] For this reason, Mandelamine is particularly suitable for chronic conditions in which permanent sterilization cannot usually be expected because of an obstruction, stone, or indwelling catheter. In such cases, Mandelamine usually renders the patient asymptomatic.

4 Although Mandelamine has been widely prescribed for more than ten years, no serious toxic effects, such as blood dyscrasias or crystalluria, have been reported. This lack of toxicity in therapeutic dosage makes Mandelamine especially useful in patients who are not under close supervision. The only contraindication is renal insufficiency.

5 Side effects, such as nausea and vomiting, are rare. Mandelamine does not cause monilial infections responsible for diarrhea, proctitis, vaginitis, and stomatitis.

6 No risk of sensitizing the patient to drugs which may be life-saving in overwhelming infections.

7 Organisms resistant to antibiotics retain their normal susceptibility to Mandelamine.[4,9]

8 In virulent infections accompanied by high fever, antibiotics or sulfonamides may exert a rapid antibacterial effect and reduce the fever. Continued therapy with Mandelamine usually brings the infection under control, while avoiding the expense and possible untoward effects of prolonged use of antibiotics or sulfonamides.

9 No supplementary acidification required (except in presence of urea-splitting organisms which are responsible for only a small percentage of urinary infections).

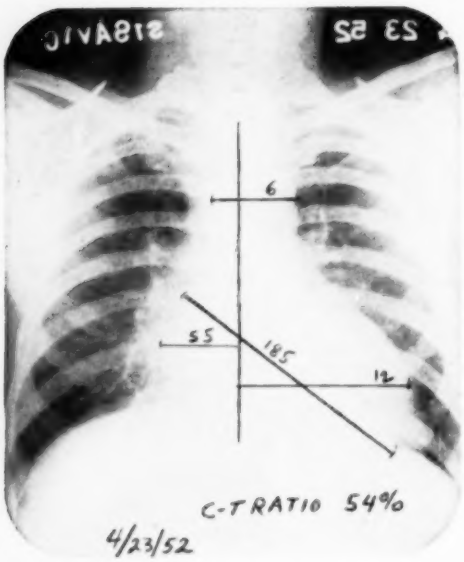
10 Regulation of diet or fluid intake is unnecessary.

11 Inexpensive.

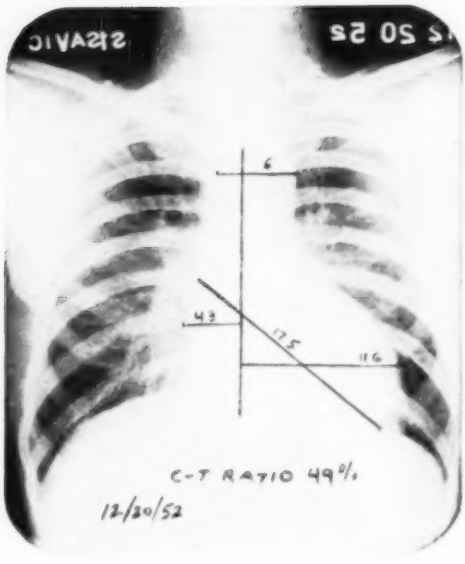
ADULT DOSAGE: 3 to 4 tablets t.i.d.
CHILDREN: in proportion.
0.25 gram enteric coated tablets, bottles of 120.

1. Beckman, H., and Tatum, A. L.: Wisconsin M. J. 51:185, 1952. 2. Carroll, G., and Allen, H. N.: J. Urology 55:674, 1946. 3. Kirwin, T. J., and Bridges, J. P.: Am. J. Surgery 52:477, 1941. 4. New and Nonofficial Remedies, A.M.A., 1953, p. 88. 5. Scudi, J. V., and Duca, C. J.: J. Urology 61:459, 1949. 6. Scudi, J. V., and Reinhard, J. F.: J. Lab. & Clin. Med. 33:1304, 1948. 7. Duca, C. J., and Scudi, J. V.: Proc. Soc. Exper. Biol. & Med. 66:123, 1947. 8. Schloss, W. A.: Connecticut M. J. 14:994, 1950. 9. Knight, V., and others: Antibiotics & Chemotherapy 2:615, 1952.

NEPERA CHEMICAL CO., INC.
Pharmaceutical Manufacturers
Nepera Park, Yonkers 2, N. Y.



Patient F.S. before Methium: Cardio-thoracic ratio 54%, blood pressure 240/160 mm. Hg.[1]



After Methium: Cardio-thoracic ratio 49%, blood pressure 160/100 mm. Hg. This patient (F.S.) experienced no toxic side effects and did not lose a single day of work.[1]

Functional improvement from stabilized, lower blood pressure

In the first few months of therapy, over 80 per cent of the patients treated with oral hexamethonium have had gradual reduction in mean blood pressure of 20 mm. Hg or more.[2,3] With continued treatment, up to or beyond a year, this reduction can often be maintained with no serious side effects and *no increase in dosage.*[2]

As blood pressure is reduced, and in some cases even without reduction, hypertension symptoms have regressed. Retinopathy may disappear, headache, cardiac failure and kidney function may improve.

Methium, a potent autonomic ganglionic blocking agent, reduces blood pressure by interrupting nerve impulses responsible for vasoconstriction. Because of its potency, careful use is required. Pretreatment patient-evaluation should be thorough. Special care is needed in impaired renal function, coronary artery disease and existing or threatened cerebral vascular accidents.

1. Kuhn, P. H.: Angiology 4:195 (June) 1953.
2. Moyer, J. H.; Snyder, H. B.; Johnson, I.; Mills, L. C., and Miller, S. I.: Am. J. M. Sc. 225:379 (April) 1953.
3. Moyer, J. H.; Miller, S. I., and Ford, R. V.: J.A.M.A. 152:1121 (July 18) 1953.

Methium®

CHLORIDE

(BRAND OF HEXAMETHONIUM CHLORIDE)

WARNER-CHILCOTT

Laboratories NEW YORK

MODERN MEDICINALS

These brief resumes of essential information on the newer medicinals, which are not yet listed in the various reference books, can be pasted on file cards and a record kept. This file can be kept by the physician for ready reference.

Achromycin, Lederle Laboratories, Pearl River, N. Y. Broad range of activity against beta hemolytic streptococcic infections, E. coli infections (including urinary tract infections, peritonitis, abscesses), meningococcic, staphylococcic, pneumococcic and gonococcic infections, otitis media and mastoiditis, acute bronchitis and bronchiolitis, actinomycosis, mixed infections and many viral and rickettsial diseases. **Dose:** As determined by physician. **Sup:** In 250 mg., 100 mg. and 50 mg. capsules, Spersoids, 50 mg. per teaspoonful (3.0 Gm.), Intravenous, 500 mg., 250 mg. and 100 mg.

Bicillin, 150,000 units, Wyeth, Inc., Philadelphia, Pa. Suspension of dibenzylethylenediamine dipenicillin G in a flavored, aqueous syrup base containing 150,000 units per teaspoonful. Treatment of Penicillin-susceptible infections in children, or as prophylaxis against rheumatic fever and secondary infection following tonsillectomy, tooth extraction or other surgery. **Dose:** As determined by physician. **Sup:** In bottles of 2 fl. oz.

Blutene Chloride-Sulfate Tablets, Abbott Laboratories, North Chicago, Ill. Tolonium chloride-sulfate. For treatment and prevention of functional uterine bleeding. **Dose:** Usual is 200 to 300 mg. daily during the course of treatment. **Sup:** In bottles of 25 and 100 tablets, (100 mg.).

Bristamin APC Tablets, Bristol Laboratories, Inc., Syracuse, N. Y. Each tablet contains Bristamin Dihydrogen citrate (equivalent to 25 mg. Bristamin base), acetylsalicylic acid, 0.21 gm.; phenacetin, 0.15 gm.; caffeine, 0.03 gm. For treatment of rhinorrhea and allergic-like symptoms accompanying the common cold. **Dose:** As determined by physician. **Sup:** In bottles of 100 and 1,000 tablets.

Calcium Disodium Versenate, Riker Laboratories, Inc., Los Angeles 54, Calif. Preparation of the calcium chelate of Ethylenediamine Tetraacetic Acid. Treatment of acute and chronic lead poisoning. **Dose:** Intravenously, as determined by physician. **Sup:** In 5 cc. ampuls, boxes of 6.

Cortef Compressed Tablets, The Upjohn Company, Kalamazoo, Mich. Brand of hydrocortisone, each tablet contains hydrocortisone, 10 mg. In rheumatoid arthritis. **Dose:** As determined by physician. **Sup:** In bottles of 25 tablets.

Darstine Tablets, Sharp & Dohme, Inc., Philadelphia 1, Pa. Brand of mepiperphenidol bromide. Anticholinergic agent recommended in the treatment of peptic ulcer and hypermotility of the gastro-intestinal tract. **Dose:** As determined by physician. **Sup:** In bottles of 50 mg. tablets.

Deltamide W/Penicillin, The Armour Laboratories, Chicago 11, Ill. Each tablet or teaspoonful contains: sulfadiazine, 0.167 Gm.; sulfamerazine, 0.167 Gm.; sulfamethazine, 0.056 Gm.; sulfacetamide, 0.111 Gm. and potassium penicillin G, 250,000 Units. In infections due to group A beta hemolytic streptococci, pneumococci, meningococci, gonococcic, some staphylococci and other

—Continued on page 63a

Upjohn

cough control plus bronchodilatation:

Orthoxicol

Trademark Reg. U. S. Pat. Off.

Each cc. contains:

Dihydrocodeinone Bitartrate 0.365 mg.
Orthoxine (methoxyphenamine,* Upjohn) Hydrochloride ..... 3.38 mg.
Hyoscyamine Hydrobromide ... 0.02 mg.
Sodium Citrate ..... 65.0 mg.

*Beta-(ortho-methoxyphenyl)-isopropyl-methylamine

Available in pint and gallon bottles

The Upjohn Company, Kalamazoo, Michigan

—Concluded from page 61a

micro-organisms sensitive to sulfonamides and penicillin. **Dose:** As determined by physician. **Sup:** Tablets in bottles of 36 and 100; suspension in bottles of 2 oz.

Erythrocin 0.2 Gm. Tablets, Abbott Laboratories, North Chicago, Ill. Erythromycin, Abbot. Indicated in pharyngitis, tonsillitis, otitis media, sinusitis, bronchitis, pneumonia, scarlet fever, erysipelas, pyoderma, certain cases of osteomyelitis and other infectious conditions. **Dose.** Average adult dose is one 0.2 Gm. tablet every 4 to 6 hours. **Sup:** This new strength is available in bottles of 25 and 100 tablets.

Geriatrone Elixir, U. S. Vitamin Corp., New York 17, N. Y. Nutritional and digestive factors especially designed for the geriatric patient. **Dose:** One-two tablespoonfuls taken with meals. **Sup:** In bottles of 16 fl. oz.

Gevrine Capsules, Lederle Laboratories, New York 20, N. Y. Vitamin, mineral and hormone product. Developed to meet older patients' requirements for vitamins and minerals needed in normal metabolism, and to provide the positive effects on protein and bone maintenance that are produced by the androgen and estrogen hormones. **Dose:** As directed by physician. **Sup:** In bottles of 100 and 1,000 capsules.

Glycine Solution, Abbott Laboratories, North Chicago, Ill. Concentrated sterile solution of glycocoll (aminoacetic acid, N.F.). For use after dilution as a urological irrigation fluid. **Dose:** As determined by physician. **Sup:** In 1,000 cc. containers, singly and in cases of 6.

Gynetone (.02 and .04) Repetabs, Schering Corp., Bloomfield, N. J. The ".02" contains 0.02 mg. ethinyl estradiol plus 5 mg. methyltestosterone, the ".04" contains 0.04 mg. ethinyl estradiol plus 10 mg. methyltestosterone. For treatment of the menopause and osteoporosis as well as for the management of geriatric patients where hormonal supplementation is desirable. **Dose:** As determined by physician. **Sup:** Repetabs ".02" and ".04" in bottles of 30 and 100 each.

Penicillin PBZ Tablets, Ciba Pharmaceutical Products, Inc., Summit, N. J. Combination of pyribenzamine with penicillin. Anti-bacterial action of oral penicillin plus minimization or prevention of penicillin sensitivity reactions. **Dose:** One 200/50 tablet every 8 hours. **Sup:** In bottles of 36 tablets in two dosage forms, 200,000 units—25 Mgm., 2000,000 units, 50 Mgm.

Potassium Chloride Emplet, Parke, Davis & Co., Detroit, Mich. Each tablet contains potassium chloride, 5 grn. In treatment of potassium deficiency. **Dose:** Two to 4 tablets 1 to 4 times daily or as directed. **Sup.:** In bottles of 100 and 1,000 tablets.

Pyraldine No. 2, VanPelt & Brown, Inc., Richmond 4, Va. Antihistaminic, decongestive cough expectorant. **Dose:** Initially, 2 teaspoonfuls followed by 1 teaspoonful every 4 hours. **Sup:** In bottles of 16 fl. oz.

Quelicin Chloride Solution, Abbott Laboratories, North Chicago, Ill. Succinylcholine chloride. For the production of muscular relaxation to facilitate endotracheal intubation, endoscopic examination and orthopedic manipulation and for the purpose of providing relaxation for general surgical procedures. **Dose:** Initial dose of 20 mg. is recommended for the average patient. **Sup:** In 10 cc. multiple-dose vials containing 20 mg. per cc. in 10 cc. ampuls containing 50 mg. per cc.

Quertine Tablets, Quertine with Ascorbic Acid Tablets, Abbott Laboratories, North Chicago, Ill. For hypertensive patients displaying a tendency to hemorrhage due to capillary dysfunction and also for use in certain other hemorrhagic syndromes, hemorrhagic diabetic retinitis, and hereditary telangiectasia. Quertine with Ascorbic Acid is offered for use in conditions in which vitamin C deficiency may coexist with capillary dysfunction. **Dose:** Ten to 20 mg. of Quertine should be given orally 3 times daily for several weeks or until the Gothlin petechial index or the rate of cutaneous lymphatic flow becomes normal. This dosage schedule is also suggested for treatment of other hemorrhagic syndromes and conditions with associated capillary dysfunction. **Sup:** In 10 mg. and 20 mg. tablets and in 10 mg. tablets with Ascorbic Acid, 50 mg.; in bottles of 100 and 1,000 tablets.

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Rauwiloid + Hexamethonium Tablets, Riker Laboratories, Inc., Los Angeles, Calif. A combination of Rauwiloid (an alkaloidal extract from Rauwolfia serpentina generically designated alseroxylon) plus hexamethonium chloride dihydrate; each tablet contains Rauwiloid 1 gm., hexamethonium 250 mg. For the treatment of severe intractable hypertension. **Dose:** Initiate therapy with ½ tablet 4 times a day not less than 4 hours apart, preferably before meals and on retiring. After two weeks, if needed, dosage may be increased by one tablet per day, but not oftener than twice weekly. **Sup:** In bottles of 100 and 1,000 tablets.

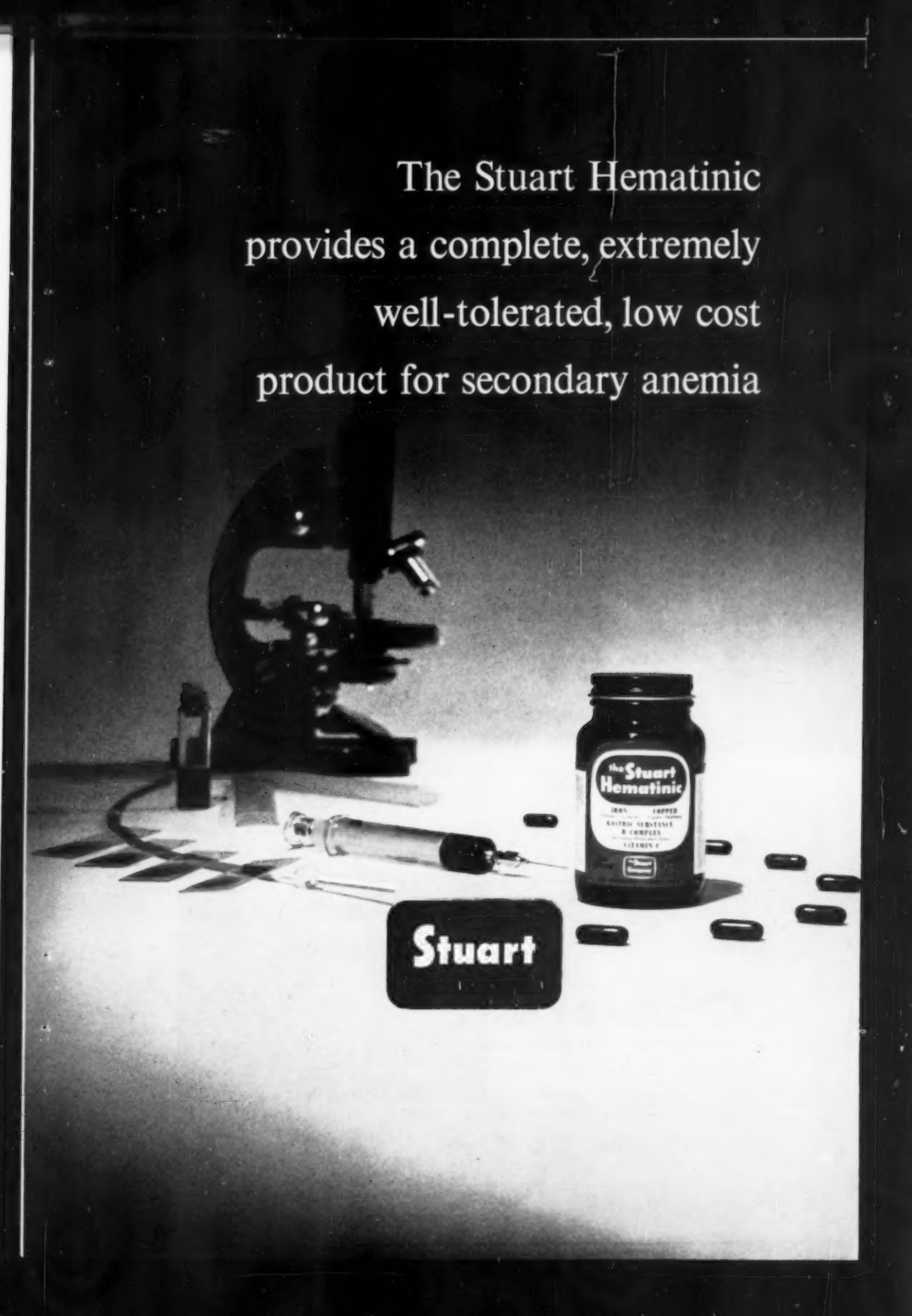
Revicaps, Lederle Laboratories, New York 20, N. Y. Each capsule contains 5 mg. of d-amphetamine sulfate and 200 mg. of methyl cellulose, in addition each capsule has vitamins A, B_1, B_2, B_6, B_{12}, C and D and minerals essential to a well-balanced diet. For the control of obesity. **Dose:** Average is 1 or 2 capsules 3 times daily ½ an hour to an hour before meals, dosage should be adjusted to the individual patient. **Sup:** In bottles of 100 and 1,000 capsules.

Syrup of 'Antepar' Citrate, Burroughs Wellcome & Co., Inc., Tuckahoe, N. Y. In pinworm infestation (enterobiasis, oxyuriasis). Contains the equivalent of 100 mg. piperazine hexahydrate per cc. **Dose:** As determined by physician. **How Sup:** In bottles of 4 fl. oz.

Tarquinor, E. R. Squibb & Sons, New York 22, N. Y. Contains 1% crude coal tar of low carbon content and 0.2% Quinolor. In treatment of common skin diseases. **Dose:** As determined by physician. **Sup:** In jars of 1 lb. and 1 oz.

Thiosulfil Suspension, Ayerst, McKenna & Harrison, Ltd., New York 16, N. Y. Contains 0.25 Gm. of sulfamethylthiadiazole in each 5 cc. For treatment of urinary tract infections. **Dose:** As determined by physician. **Sup:** In bottles of 4 and 16 fl. oz. (new form) as well as in bottles of 100 and 1,000 tablets (0.25 Gm.).

The Stuart Hematinic
provides a complete, extremely
well-tolerated, low cost
product for secondary anemia



Great Potency

in tiny form

the therapeutic multivitamin tablet with B_{12} and Synthetic A

SMALLEST of its kind, an OPTILET provides potent, new advantages in vitamin therapy. Each easy-to-swallow tablet contains therapeutic amounts of six synthetic vitamins plus B_{12}. Since OPTILETS have synthetic vitamin A, there are no allergic reactions, no fishy after-taste, no "burp." Because they are tablets—not capsules—they can't leak, won't stick together. Therapeutic dose is one OPTILET or more daily. Cost no more than ordinary therapeutic formula vitamins. OPTILETS are available in bottles of 50, 100 and 1000 tablets. Abbott

Optilets®

(Abbott's Therapeutic Formula Vitamin Tablets)

among the candidates for COMBANDRIN*

PROTEIN ANABOLIC STEROID HORMONE COMBINATION

...tired elderly patients

With Combandrin, the tired, elderly patient lacking the metabolic support supplied in earlier years by gonadal hormones can often be made stronger, more alert. Formation and retention of protein are promoted, aging bone can be given a "new lease" on life, and mental and emotional reactions may be favorably influenced. More persons can "live"—not merely exist—in their sixties, seventies and eighties. For, the overall results of Combandrin therapy (balanced androgen-estrogen steroid therapy) in the aged "is a lessening of the degenerative state . . ."

Kountz, W. B.: Ann. Int. Med. 35:1055, 1951.

SUPPLIED: Each cc. contains 1 mg. estradiol benzoate and 20 mg. testosterone propionate in sesame oil, for intramuscular injection. In single-dose disposable Steraject® cartridges and in 10 cc. multiple-dose vials.

Also, Combandrets® — androgen-estrogen combination in convenient tablet form for absorption by transmucosal route.

PFIZER SYNTEX PRODUCTS

Pfizer

PFIZER LABORATORIES, *Brooklyn 6, N. Y.*

DIVISION, CHAS. PFIZER & CO., INC.

*TRADEMARK

new
Privine Nebulizer

convenient
effective

Now, at work or play,
patients with stuffy noses
can carry the
new Privine Nebulizer
in purse or pocket.
They *spray* so they
can breathe comfortably.
The fine mist penetrates
into the nasal passages
for *relief of nasal congestion—*
potent, prompt, prolonged

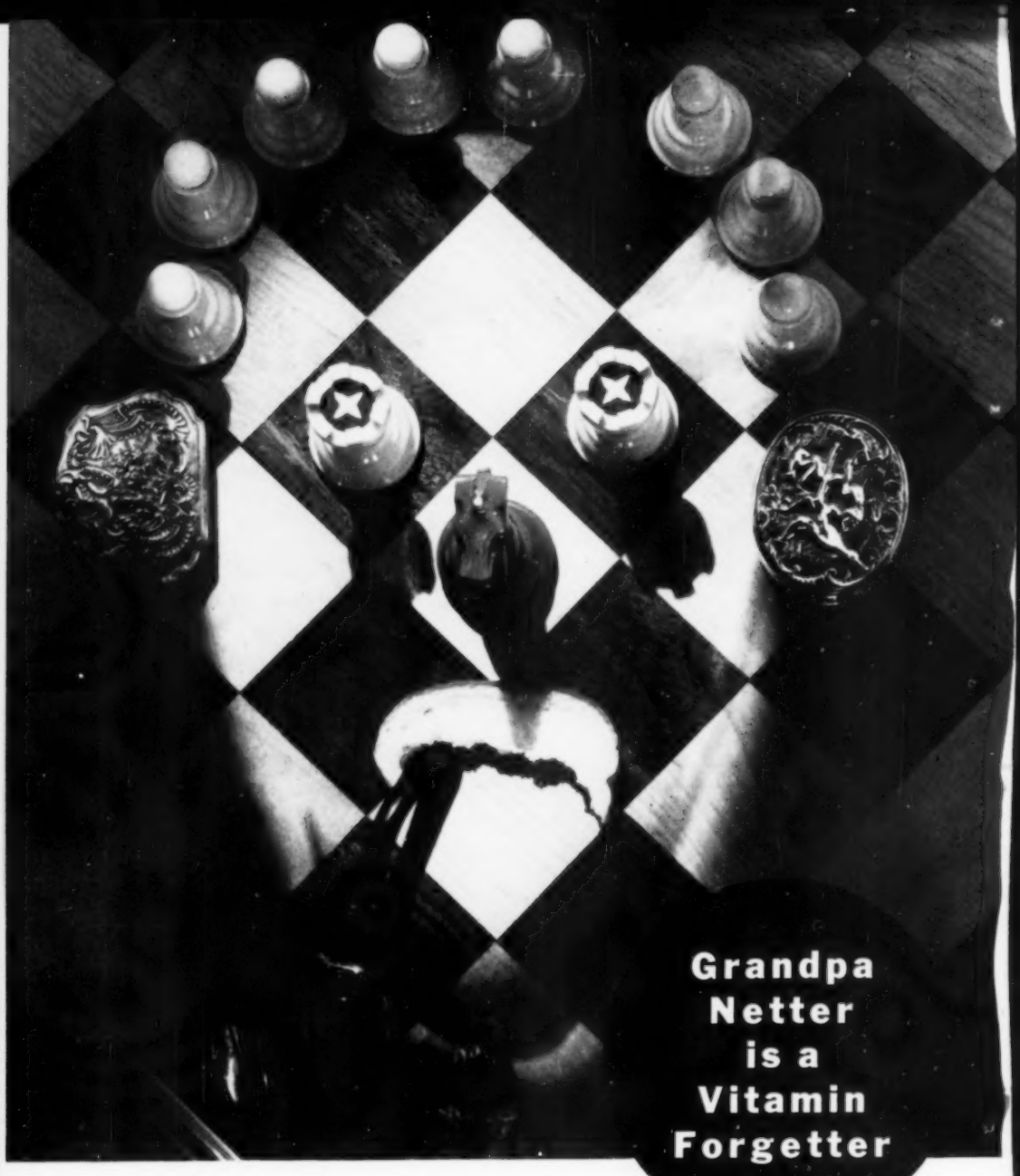
Privine® Nebulizer

15 cc. of 0.05 per cent solution.
Same composition and
therapeutic advantages as
Privine Nasal Solution
widely prescribed in
drop dosage.

Ciba *Summit, New Jersey*

PRIVINE® HYDROCHLORIDE (NAPHAZOLINE HYDROCHLORIDE CIBA)

2/1843M



Grandpa Netter is a Vitamin Forgetter

Aging, sedentary, forgetful . . . is it any wonder he forgets proper nutrition? Like so many others, he needs a new dietary *and* DAYALETS—the fishless burpless multivitamins. Synthetic A plus nine other important vitamins. No fish-oil taste or odor, no allergies due to fish oils. How about *your* vitamin deficients?

Abbott

Dayalets®

(ABBOTT'S MULTIPLE VITAMINS)

Each DAYALET tablet represents:

→ Vitamin A (Synthetic)	10,000 U.S.P. units
Vitamin D	1,000 U.S.P. units
Thiamine Mononitrate	5 mg.
Riboflavin	5 mg.
Nicotinamide	25 mg.
Pyridoxine Hydrochloride	1.5 mg.
Vitamin B_{12}	2 mcg. ←
→ Folic Acid	0.1 mg.
Pantothenic Acid	5 mg.
Ascorbic Acid	100 mg.

Abnormalities in Fluid Balance When There Is A Failing Heart

ARTHUR C. GUYTON, M.D.*
University, Miss.

The term "failing heart" means many different things to different clinicians. Some think of a failing heart as one which is failing to deliver a sufficient cardiac output, whereas others have the idea that a failing heart is one that causes intense signs of peripheral or pulmonary congestion. Indeed, all of these different definitions of a failing heart are quite correct, but there are times when a heart can be failing and yet the cardiac output may be several times normal rather than below normal. Also, there are times when the heart may be failing while at the same time the peripheral or pulmonary venous pressure might be well within the range of normal or even below normal.

From the point of view of the physiologist, a failing heart is a heart that is not pumping all of the blood that is being returned to it without causing excessive rise of the input venous pressure to the heart. In other words, according to Starling's Law of the Heart, under normal conditions the heart pumps all of the blood which comes to it, and it does so without any major rise in venous pressure. When the heart fails to pump all the blood that comes to it without excessive rise in venous pressure, then it no longer obeys Starling's Law, and it is failing.

Actually, the heart is composed of four different pumps including the two major pumps, the ventricles, and the two primer pumps which are the auricles. The left auricle and the left ventricle form a two-stage pump system and so do the right auricle and the right ventricle. It is not correct to speak simply of heart failure, for one should properly speak of failure of the left or of the right heart, for each of these two heart systems is to more or less degree separate from each other. There are reasons, however, why one usually considers, clinically, both sides of the heart together when he speaks of failure. Whenever there is diffuse disease of the heart, it ordinarily affects both sides of the heart at the same time. Furthermore, if either side of the heart begins to fail and the cardiac output of the entire heart decreases, this can decrease the coronary blood supply and cause failure of the opposite side of the heart. Finally, the two sides of the heart are bound together by the septum between the

*From the Department of Physiology and Biophysics, School of Medicine, University of Mississippi, University, Mississippi.

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two sides. Consequently, if one side of the heart is not beating with its usual force, the septum is likely to flutter the wrong direction during the beat of the heart and thereby affect the side of the heart which was not originally failing. Therefore, it is rare for one side of the heart to fail without the other side failing concomitantly.

There are occasional times when one side of the heart exhibits acute signs of failure while the other side of the heart is still functioning relatively normally. This can occur when a serious, acute infarct occurs in the myocardium of only one side of the heart. Pathologically, it has been found that such as this occurs approximately 30 times as often in the left heart as in the right heart. Nevertheless, in order to understand all of the ramifications of fluid shifts in heart failure, it is necessary to discuss failure of each side of the heart separately. It will be pointed out subsequently that the fluid shifts which occur are dependent to a great extent upon which side of the heart does fail predominantly.

A. Fluid Shifts Following Acute Failure of the Left Side of the Heart It has been shown in experimental animals, and it can also be deduced from logical considerations, that acute failure of the left side of the heart causes damming of blood in the pulmonary venous system. If the right heart is still pumping blood essentially normally, large quantities of blood will continue to be pumped into the pulmonary system, but there will be far greater difficulty than normally for this blood to pass out of the lungs, through the left heart, and back into the systemic circulatory system. Consequently, all of the pressures in the entire pulmonary vascular tree increase as a result of acute failure of the left side of the heart. All the vessels of the pulmonary vascular tree expand in size, and large quantities of blood collect in the lungs. Therefore, the primary effect of acute left-sided failure of the heart is *pulmonary congestion.* When extremely large quantities of blood collect in the vessels of the lungs, the fluid pressure within the capillaries increases to such an extent that some of the fluid exudes into the tissue spaces of the lungs and into the alveoli. This is the cause of pulmonary edema and hypostatic pneumonia in patients with acute left-sided heart failure.

A second consequence of acute left-sided heart failure, a consequence which is not so easily understood immediately, is a shock-like condition which may occur in the systemic circulatory system. If blood shifts into the lungs to cause pulmonary congestion, this blood must come from some other part of the circulatory system. Indeed, it appears from animal experiments that at least 500 to 1000 cc. more blood than normal can enter the lungs in acute failure of the left side of the heart.[1] If this much blood is suddenly lost from the peripheral circulatory system, it decreases the filling pressure of blood in all of the vessels of the systemic system. Recent studies from our laboratory have indicated that it is this filling pressure of blood in the systemic vessels that is mainly responsible for the return of blood to the heart. (The greater the quantity of blood, other factors remaining neutral, in the systemic vessels, the greater will be the filling pressure of the blood in these vessels and the greater will be the pressure gradient from the average systemic vessel to the right atrium where the pressure is essentially zero.[2] Consequently, blood flows readily from well-filled systemic vessels to the low pressure area of the heart.) In the case of acute failure of the left side of the heart with concomitant shift of blood to the pulmonary system, the filling pressure of the systemic vessels is greatly decreased, and for obvious reasons the return of blood to the heart is also greatly decreased.

It is quite obvious that the decrease in return of blood to the heart in acute left

heart failure causes a decrease in cardiac output.

It has been found in a number of clinical cases that patients exhibiting predominantly acute failure of the left side of the heart occasionally have low peripheral venous pressures. This seems to be a paradox because most clinicians associate heart failure with a high venous pressure. However, from logical considerations, acute failure of the left side of the heart without any concomitant failure of the right side of the heart *should* cause a low peripheral venous pressure. When a large quantity of blood shifts into the pulmonary system and the venous return to the heart decreases, as was explained above, this, logically, decreases the venous pressure if the right heart is still pumping normally. The reason why a low venous pressure is not seen more often in acute failure of the left side of the heart is that the right side of the heart usually fails at the same time.

B. Changes in Fluid Dynamics Resulting from Acute Failure of the Right Heart If the left side of the heart continues to pump blood normally but the right side of the heart suddenly fails, this means that blood is not being pumped from the systemic circulatory system into the lungs normally, but it is being pumped perfectly normally from the lungs into the systemic system. In other words, blood is being dammed in the peripheral venous system. It was pointed out above that left heart failure occurring while the heart is pumping normally always causes a large shift of fluid from the systemic circulatory system into the lungs. The opposite effect occurs when the right side of the heart fails. However, there is only about 1 liter of blood to begin with in the two lungs. Consequently, the quantity of fluid shift from the lungs into the systemic circulatory system is of minor consequence. Even if as much as 500 cc. of blood, which is doubtful, should shift from the lungs to the systemic circulatory system, this would hardly change the various pressures in the different vessels of the systemic system because the systemic system is tremendous in volume in comparison to the pulmonary system.

In essence, it has been found experimentally and in human patients that acute failure of the right heart never causes intense congestion of the peripheral veins but usually causes only 4 to 7 mm. Hg. rise in peripheral venous pressure.[3] It will be noted subsequently that prolonged failure of the right heart causes very intense peripheral congestion, but, for the time being, suffice it to say that acute failure of the right heart causes only mild peripheral congestion for the simple reason that the amount of fluid which is shifted from the lungs into the peripheral circulatory system is not sufficient to cause significant congestion.

The major effect of acute failure of the right heart is an intense decrease in cardiac output. It was discussed above that when there is excess blood in the vessels of the systemic circulatory system, this causes an increase in the filling pressure of all of these vessels, and it is this filling pressure which causes the blood to flow toward the heart where the right atrial pressure is usually about 0 mm. Hg. Experiments from this laboratory indicate that the normal mean filling pressure of the systemic circulatory system is approximately 5 to 8 mm. Hg. and that this mean filling pressure can rise aproximately to 12 to 14 mm. Hg. as a result of sympathetic stimulation.[4] In other words, normally, there is approximately a 5 to 8 mm. pressure drop from the average peripheral vessel to the heart, and it is this 5 to 8 mm. of pressure which is causing blood to return to the heart. If the pressure in the right auricle rises to 4 to 7 mm. Hg., as it does when the right heart is damming up blood, then the pressure gradient from the mean filling pressure of the peripheral vessels to the heart is considerably reduced. Sympathetic stimulation, of

course, compensates for some of this decrease in pressure gradient but does not compensate entirely. Consequently, the return of blood to the heart may be greatly decreased as a result of acute failure of the right heart. Obviously, this causes a tremendous decrease in the cardiac output.

Summarizing, the major effect of acute failure of the right heart is an intense decrease in cardiac output with essentially no other abnormal functions of the circulatory system.

C. The Effects of Concurrent Failure of the Two Sides of the Heart It has been noted above that failure of either the left side of the heart or of the right side of the heart can cause a decreased cardiac output. The reason for this decreased cardiac output is different in left heart failure from right heart failure: left heart failure decreases the filling pressure of the systemic circulatory system while right heart failure increases right atrial pressure and, therefore, opposes the return of blood in this manner. When there is combined failure of both sides of the heart, a combination of these two factors is likely to cause greater than ever decrease in cardiac output. Consequently, regardless of what type of acute heart failure occurs, one of the most predominant effects is a decrease in cardiac output.

It was noted that acute left heart failure can cause extreme pulmonary congestion and acute right heart failure can cause mild peripheral congestion. The reason for these effects is, obviously, a shift of fluid from one system to the other. If there is approximately equal failure of the right heart and the left heart, there will be very little shift of fluid from one system to the other. Consequently, right heart failure actually diminishes the amount of pulmonary congestion which occurs from left heart failure. On the other hand, left heart failure also diminishes the mild peripheral congestion which occurs as a result of acute right heart failure. Obviously, there occur all different degrees of combined left and right heart failure, and as noted in the introduction to this paper, it is very rare for one side of the heart to fail entirely to the exclusion of the other side.

D. Autonomic Reflexes in Response to the Failing Heart Any time that the cardiac output begins to decrease there occurs a tendency for the blood pressure to fall, and there also occurs ischemia of many vital centers of the body. When the blood pressure falls even slightly, this initiates pressoreceptor reflexes from the carotid sinuses and from the large arteries of the chest. These pressoreceptor reflexes cause the vasomotor center in the medulla to send a tremendous outflow of sympathetic impulses to the entire vascular bed and to the heart. It has also been shown that ischemia can cause the outflow of many sympathetic impulses from the vasomotor center. This results from two factors: first, ischemia directly affects the vasomotor centers to increase the outflow of sympathetic impulses; second, ischemia causes increased activity of the chemoreceptors in the carotid and aortic bodies. Increased activity of these chemoreceptors causes impulses to pass to the medulla where the excitability of the vasoconstrictor centers is increased. Consequently, there are both ischemic and pressure reflexes which become active when the cardiac output decreases, and both of these reflexes cause a greatly increased outflow of sympathetic impulses to the vascular system and to the heart.

The sympathetic impulses to the heart, obviously, increase the rate of contraction of the heart. Recent studies in our laboratory indicate that these sympathetic impulses also increase the force of contraction of the undamaged portions of the heart by approximately 50 to 60 per cent.[5] In other words, the autonomic reflexes to the heart during failure tend to

increase the efficiency of the heart both by increasing the strength of contraction of the remaining active fibers of the heart and by increasing the rate of the heart.

Sympathetic impulses to the vascular tree cause constriction of both the arterial vascular bed and the venous vascular bed. Constriction of the arterioles, in particular, is responsible for the maintenance of a more or less normal blood pressure even though the cardiac output may be decreased by 50 per cent or more in many patients with acute heart failure. It should be noted specifically that the sympathetic impulses which constrict the arterioles do not affect the small arteries and arterioles either of the coronary vessels or to a great extent of the brain. Indeed, the sympathetic impulses to the coronary vessels cause an increase in dilatation of the coronaries, thereby supplying the heart with perhaps an almost normal blood supply. Fortunately, the poor sympathetic vasoconstrictor effect on the cerebral vessels results in only a few per cent diminishment of blood supply to the brain. Consequently, there occurs little or no cerebral damage as a result of the sympathetic reflexes.

Sympathetic constriction of the venous bed of the circulatory system causes an increase in the filling pressure within the tremendous venous vascular tree. Because the veins of the body contain the major proportion of the body's blood, this increased filling pressure within the veins causes much more rapid return of blood to the heart than would have occurred normally. Consequently, the sympathetic reflexes partially overcome the decreased filling pressure resulting from shift of fluid from the systemic circulatory system into the lungs in acute left heart failure, and it partially overcomes the diminished gradient of blood flow from the veins to the right heart when there is increased right auricular pressure as the result of acute right heart failure. Therefore, the autonomic reflexes initiated by decreased cardiac output tend, in several ways, to correct the diminished cardiac output.

Fortunately, the autonomic reflexes are very rapid in becoming active when the heart begins to fail. Indeed, these reflexes reach their maximum state of activity in less than one minute. From a clinical point of view it is these reflexes which cause the pallor of the skin, the coldness of the skin, the associated sweating that frequently occurs, and the very fast pulse rate of the heart which is usually observed in acute cardiac failure.

E. The Effect of Decreased Cardiac Output on Capillary Dynamics

Experiments first performed by Starling some 60 years ago[6] and extended by Starr approximately a dozen years ago,[7] and, finally, re-investigated and further extended in our laboratories during the past few years[2, 4] indicate that a decreased cardiac output, other factors remaining constant, causes a decrease in capillary pressure. The reason for this is as follows: when the heart does not put out a sufficient quantity of blood, either the arterial pressure falls or tremendous arteriolar constriction occurs. In either instance the pressure at the arterial end of the capillary is certain to fall considerably. On the other hand, if the heart is not pumping sufficiently, this causes a rise in venous pressure. The question is: which is more important so far as the capillaries are concerned, the decrease in pressure at the arterial end of the capillary or the rise in pressure at the venous end? All of the experiments thus far conducted indicate that the decrease in arterial pressure exerts more influence on the capillary dynamics than does the rise in venous pressure. Consequently, a failing heart apparently first causes decreased capillary pressure.

It has been shown many times that a decreased capillary pressure results in an increase in the blood volume. The reason for this is that the colloid osmotic pressure of the proteins in the plasma is

normally balanced by the capillary pressure. The normal capillary pressure causes fluid to leave the capillaries while the colloid osmotic pressure causes it to enter. Consequently, when the capillary pressure becomes decreased below normal, this, theoretically, should cause fluid to flow from the interstitial fluid spaces into the capillaries as a result of greater colloid osmotic pressure than capillary pressure. This, apparently, is the case, for, immediately after the cardiac output is decreased as the result of cardiac failure, the blood volume begins to increase and continues to increase for many days.

F. The Effects of a Decreased Cardiac Output on Kidney Function It is a well-known fact that acute failure of the heart with decreased cardiac output results in immediate oliguria or even, in many patients, anuria. The reason for this appears to be the tremendous outflow of sympathetic impulses fom the vasoconstrictor centers of the medulla. It has been shown that a generalized sympathetic discharge from the medulla affects the afferent arterioles of the kidneys as much as or more than it affects any other arterioles of the body.[8] Consequently, sympathetic discharges cut off the flow of blood almost entirely to the glomeruli of the kidneys and thereby diminish the filtration of fluid into Bowman's capsule to such an extent that the patient becomes either anuric or oliguric.

The oliguria which occurs consequent to acute failure of the heart lasts from 3 to 4 days to as long as several weeks.

It will be noted subsequently that oliguria leads to various effects in the circulation which in themselves tend to avert the oliguria. In other words, the retained fluid increases the blood volume, and this in turn causes the cardiac output to return toward normal and, therefore, increase the output of the kidney back toward normal.

G. Increased Blood Volume in Response to Decreased Cardiac Output It was pointed out above that a decreased capillary pressure as a result of decreased cardiac output can cause blood to flow from the interstitial fluid spaces into the blood. It has been shown in a number of different laboratories that the quantity of fluid in the interstitial spaces which can be displaced from these spaces into the blood is very slight.[9, 10] Our own studies indicate that the total quantity of such fluid is probably no greater than 300 to 500 cc. in the average adult.[11] Consequently, the blood volume cannot increase greatly simply as the result of decreased capillary pressure, and, indeed, the increase in blood volume resulting from this effect is probably so slight that the usual methods for interpreting blood volume could hardly be expected to prove that such actually occurs. On the other hand, the retained fluid in the blood stream as a result of oliguria can very readily cause an increase in blood volume. Furthermore, it has been shown that a patient in cardiac failure has a natural desire to drink water and to some extent even desires salty water. This, combined with the initially decreased capillary pressure in the villi of the intestinal tract, results in increased absorption of water and salts into the circulatory system.

It has been shown many times that, as a result of all the factors combined, the blood volume increases tremendously during the first week to ten days following very severe acute failure of the heart.

H. Increased Red Blood Cells in the Blood in Response to Decreased Cardiac Output Physiologically, any time there is ischemia in the body there occurs an increased formation of red blood cells by the bone marrow. It has long been believed that the bone marrow is directly responsive to anoxia whether this anoxia be due to anoxic anoxia, anemic anoxia, stagnant anoxia, or histotoxic anoxia. However, this has not been proved, and it is possible that ischemia of

some other part of the body relays a hormonal factor to the bone marrow or otherwise causes the bone marrow to increase the production of red blood cells. Nevertheless, from a practical point of view, so far as the circulatory system is concerned, the decreased cardiac output during cardiac failure with resultant bodily ischemia does cause an increase in the number of red blood cells circulating in the blood. Indeed, the hematocrit may rise from a normal or 40 to 45 up to values as high as 50 to 60 per cent. This, combined with a considerably increased blood volume, means that the actual total red cell mass of the circulatory system sometimes increases to as much as two times normal as a result of the decreased cardiac output during cardiac failure.[12] Obviously, the increased number of red blood cells partly compensates for the decreased cardiac output.

I. Return of Cardiac Output Toward Normal as the Result of Increased Blood Volume As the blood volume increases following cardiac failure, this increases the amount of blood in all the vessels of the circulatory system and consequently increases the filling pressure of these vessels. Indeed, it has been shown that the mean filling pressure of the blood vessels of the systemic circulatory system during cardiac failure can increase as much as 100 per cent or more. As noted above, it is this filling pressure of the vessels in the systemic circulatory system which causes the blood to flow toward the low pressure area of the right auricle. Consequently, as the blood volume increases, more blood flows toward the heart causing an increased venous return and an increased cardiac output.

It is quite obvious from the above discussion of sequential developments in fluid retention in the body that decreased cardiac output initiates a series of changes in the fluid balance of the body which finally ameliorates the decreased cardiac output. This is one of the most important physiological compensations which occurs in response to failure of the heart.

J. Edema as the Result of Decreased Cardiac Output The valuable aspects of fluid retention resulting from oliguria and from increased absorbability of fluid and salts by the gastrointestinal tract have been pointed out above. Unfortunately, not all of this fluid is retained in the circulatory system. Approximately 4/5 of the fluid passes immediately from the circulatory system into the tissue spaces, and only approximately 1/5 remains within the vascular bed even for the first few hours.[13] Therefore, the very important physiological compensation of increased filling pressure of the circulatory system is always accompanied by a certain amount of edema. This is an unfortunate circumstance and sometimes the edema is more detrimental to the patient than had been the decreased cardiac output which was ameliorated to some extent by fluid retention.

In many patients the edema which results as a consequence of fluid retention is not very great and is not a bothersome problem. The reason for this, it appears, is that the increased cardiac output consequent to fluid retention is often sufficient to overcome the oliguric effect of low cardiac output on the kidneys, and the kidneys begin to function relatively normally once again. Therefore, the edema does not continue developing.

The patient with a failing heart is usually treading a very thin margin of safety so far as edema is concerned, for, if the cardiac output does not return almost back to normal, then the output of urine from the kidney may never return to normal or even within range of normal. Consequently, such a patient may continue to retain fluid in his circulatory system indefinitely. Up to a certain extent increased blood volume apparently is valuable to cause increased return of blood to the heart, but, eventually, too

much return of blood to the heart can cause excessive dilation of the heart and increased failure of the heart muscle. Also, as the vascular bed becomes progressively more and more filled with blood, less and less of the increments of fluid retained by the kidneys remain within the blood stream and more and more go into the interstitial fluid spaces.

K. Compensated and Decompensated Heart Disease The term, compensated heart disease, means a patient who shows no obvious outward signs of heart failure. It does not mean that the heart itself may not be failing because there are many patients who have compensated heart disease who at the same time have greatly decreased cardiac outputs or perhaps have to some extent abnormally increased pulmonary venous pressure or increased peripheral venous pressure. In general, the major outward sign of cardiac failure is inordinately increased edema, either edema of the lungs or edema peripherally. Therefore, a patient is usually said to be compensated when he has no outward signs of either pulmonary or peripheral congestion, whereas he is said to have uncompensated heart disease when he has excessive quantities of either pulmonary or peripheral edema.

It was noted above that the patient with cardiac failure treads an extremely thin margin of safety insofar as edema is concerned. When the heart failure is not too severe, the physiological compensatory mechanism of increased blood volume and the autonomic reflexes can many times return the cardiac output to sufficiently near normal that the kidneys can excrete all of the fluid and salts which are taken in by mouth. In this instance the patient will not continue to develop progressively more and more edema. On the other hand, if the failure of the heart increases only a slight amount more, then the output of fluid by the kidney cannot keep up with the intake, and the patient will go into a state of uncompensated heart disease.

L. Special Features of Chronic Left Heart Failure The basic symptom of chronic left heart failure is, as with acute left heart failure, pulmonary congestion. However, this pulmonary congestion is likely to be greatly exacerbated during chronic failure over and above the congestion occurring during acute left heart failure. The reason for this is the retained fluid which has occurred as a consequence of decreased cardiac output. Many patients with acute left heart failure live through the first week to ten days of their disease and then without any increase in the actual failure of the heart to pump, die as a result of increased pulmonary congestion.[14] Obviously, the initial pulmonary congestion resulting from left heart failure is due to a shift of blood from the systemic circulatory system into the lungs. There is a limit to the quantity of blood which can be shifted from the systemic circulatory system into the lungs because, as this blood is shifted into the lungs, the return of blood to the right heart from the systemic circulatory system progressively diminishes, and the output of blood from the right heart to the lungs is considerably decreased as a result. After a few days of retaining fluid in the circulatory system in response to the low cardiac output, the quantity of blood in the peripheral circulatory system rises back to normal or approximately normal, and the quantity of venous return to the right heart approaches normal. Consequently, the quantity of blood pumped through the right heart into the lungs progressively increases as a result of this physiological compensatory mechanism. Because the left heart is still failing to pump blood and because the right heart is pumping more blood than immediately after the acute attack of left heart failure, the total quantity of blood dammed in the lungs progressively increases as more fluid is retained by the kidneys, and the patient

experiences progressively increased dyspnea and perhaps death as a result.

M. Special Features of Chronic Right Heart Failure In acute right heart failure the degree of peripheral congestion is extremely slight because only a small amount of blood can be shifted from the lungs into the peripheral circulatory system in order to cause such congestion. However, in response to the decreased cardiac output, the progressive increase in blood volume changes the mild peripheral congestive symptoms into severe peripheral congestive symptoms. As with chronic left heart failure, the increase in blood volume may cause such greatly increased venous return that the cardiac output returns to normal or almost normal. Nevertheless, there remain the severe symptoms of peripheral congestion, and it is these symptoms which are particularly peculiar to chronic right heart failure. It should be pointed out, also, that edema does not occur immediately after the right heart acutely fails but develops gradually during the ensuing days along with the greatly increased symptoms of peripheral congestion. Consequently, peripheral edema is generally considered to be a part of the peripheral congestive picture.

N. A Physiological Classification of Heart Failure From the preceding discussion it will have been noted that there are three major classes of symptoms which are noted clinically in response to heart failure: First, in acute failure of either the left heart or the right heart there is a greatly decreased cardiac output. Second, in either acute or chronic failure of the left heart there occurs pulmonary congestion of all degrees of severity. Third, in chronic right heart failure there occur very severe peripheral congestive symptoms. Therefore, from a physiological point of view, three clinical types of heart failure can be classified quite readily according to the types of symptoms which result: first, cardiac failure with low cardiac output; second, cardiac failure with pulmonary congestion; and, third, cardiac failure with peripheral congestion. It will be noted that under special conditions any one of these three different types of clinical cardiac failure can occur exclusive of the other two. For instance, cardiac failure with low cardiac output can occur with no clinical signs of pulmonary or peripheral congestion in pure acute right heart failure. Secondly, cardiac failure with pulmonary congestion can occur without either of the other two in chronic left heart failure. Finally, cardiac failure with severe peripheral congestive symptoms can occur without symptoms either of pulmonary congestion or symptoms of low cardiac output in chronic right heart failure.

From a clinical point of view, the three different physiological types of heart failure usually occur in various combinations. Furthermore, immediately after an acute heart attack, there might be heart failure with low cardiac output, and this might change gradually during the ensuing days into heart failure of one of the other two types or into a combination of the various types of heart failure.

It is valuable from the clinician's point of view to determine the extent to which each of the three different types of conditions exists in cardiac failure—namely, low cardiac output, pulmonary congestion, and peripheral congestion—for the type of treatment depends essentially upon this evaluation by the clinician.

O. Treatment of Low Cardiac Output Heart Failure If a patient has chronic heart failure and still has a low cardiac output despite a greatly increased blood volume and despite extreme autonomic sympathetic discharges throughout his body, then there is very little that can be done for the patient unless there is some way to revert the actual lesions within the heart which are causing the heart failure. Obviously, such drugs as the digitalis alkaloids can, in many instances, bet-

ter the function of the heart and, therefore, correct the low cardiac output which exists under these conditions.

When low cardiac output occurs in acute heart failure, the cause of the low cardiac output appears in many patients to be decreased venous return to the heart (caused by shifts of fluid into the lungs in the case of left heart failure and caused by a mildly elevated right auricular pressure in the case of acute right heart failure.) In either of these instances, if the blood volume can be increased rapidly enough to increase the mean filling pressure of the systemic blood vessels, the return of blood to the heart will be increased. Consequently, it has been found that in many patients with acute heart failure exhibiting signs of low cardiac output, the output of the heart can be greatly increased by transfusing the patient. This fact has been shown in numerous experiments in this laboratory[15] and has been tried in a number of clinical centers.[16,17] Schwartz has pointed out that the quantity of blood or plasma which must be transfused in order to save the life of a patient in such instances is extreme — perhaps as much as 1500 to 2000 cc.[17]

Even though transfusions have been successful in saving the lives of a few patients having acute heart failure with low cardiaic output, such a practice certainly is not to be recommended universally, for transfusing such a patient, should he have acute left heart failure, may very well cause death of the patient as a result of pulmonary congestion. If the clinician is fortunate enough to be treating one of the rare patients who has essentially no left heart failure but only acute right heart failure, transfusion is almost certainly the advisable procedure, for the increase in peripheral congestive symptoms which is likely to result from transfusion is of minor consequence in comparison with the likelihood of death due to cardiac shock because of low cardiac outpnt.

It is extremely difficult to determine immediately whether the dyspnea which occurs in the patient with acute heart failure is due to low cardiac output or due to pulmonary congestion. If the auscultatory signs of pulmonary congestion are slight in comparison with the dyspnea, it is probable that the dyspnea is due mainly to stagnant anoxia, and transfusion would be likely to alleviate some of the symptoms and save the life of the patient. On the other hand, if the signs of pulmonary congestion are extreme, then it is equally as likely that transfusion might cause death of the patient. It, therefore, is an extremely difficult problem for the clinician to decide whether or not to transfuse the patient in cardiac shock as a result of acute heart failure. Nevertheless, it is probably better to take a chance on transfusion rather than to allow the patient to die of shock.

P. Treatment of Pulmonary and Peripheral Congestion In general, the treatment of pulmonary and peripheral congestion is essentially the same in each instance. In essence, both of these types of congestion are due to too much fluid at the wrong place at the wrong time. The theory of treatment is simply to decrease the total quantity of fluid in the circulatory system. The drastic method for decreasing this in a patient who has severe pulmonary congestion is venesection. Also, in the case of pulmonary congestion this can be treated by causing increased congestion in certain peripheral parts of the body—that is, placing tourniquets on the various limbs of the body can cause increased congestion in these areas and thereby remove some of the blood from the general circulatory system and from the pulmonary vascular bed.

For long-term treatment of pulmonary and peripheral congestive symptoms the problem is mainly one of a balance between fluid intake and fluid output. Usually it has been found that decreased sodium intake is the most important fac-

tor in the control of the balance between fluid intake and fluid output. The greater the quantity of sodium ingested by the patient, the greater is the quantity of retained fluid. Exactly why this occurs is not definitely known, but it is probably partly related to the activity of the posterior pituitary gland. When the level of sodium intake is increased and the kidney is unable to excrete this sodium, the total level of ions in the extracellular fluids increases. This causes a greater than normal crystalloidal osmotic pressure in the extracellular fluids. It has been shown many times that increased crystalloidal osmotic pressure causes the osmoreceptor neuronal cells of the hypothalamus to send an increased number of impulses to the posterior pituitary. This gland, in turn, secretes the antidiuretic hormone which causes far greater than normal reabsorption of water by the distal tubules of the kidneys. Thus, excessive intake of salt, which salt is not excreted by the kidneys, causes a concomitant retention of water by the kidneys. On the other hand, if the salt intake is limited, this posterior pituitary mechanism does not come into play, and no more water is retained than that quantity needed to cause an isotonic solution of the salt which is available. Therefore, ordinarily, it is not necessary to restrict the water intake of a congestive patient as long as the salt intake is restricted. Indeed, because restricted water intake is likely to lead to kidney infection, it is probable that such should be discouraged except in special instances of very severe combined cardiac and kidney failure.

Also in the armamentarium of the clinician for the treatment of excessive fluids during cardiac failure are the many diuretics. When the heart is so weak that the cardiac output, even in response to an increased blood volume, never returns sufficiently high to cause almost normal kidney function, often it is almost impossible, even with salt restriction, to keep the intake of fluid and salts equal to the output by the kidneys. Under these conditions not only must the intake of salts be restricted, but the kidneys must be helped in their function of ridding the body of fluid by the use of diuretics. It is obvious that mild cases of cardiac failure can be treated by use of the mild diuretics, notably the xanthines. On the other hand, when cardiac failure becomes severe and the cardiac output becomes progressively more and more diminished, the kidney's inability to excrete sufficient quantities of water and salt is so great that only the very powerful diuretics can be effective, notably the mercurials. Physiologically, the xanthine diuretics, if they are adequate, are far more physiological in their activity on the kidneys than are the mercurials, for the xanthines cause diuresis by promoting vasodilation of the afferent arterioles to the glomeruli. This increases the glomerular pressure and thereby increases the rate of filtration into the tubules. The glomerular filtrate passes thence through the tubules where normal reabsorptive processes occur, and electrolyte balance of the extracellular fluids of the body is maintained essentially normal. On the other hand, the mercurial diuretics perform their function by preventing reabsorption of water and salts by the tubules. Actually, mercurial diuretics cause a certain amount of denaturization of the proteins within the living cells of the tubules. Because it is these cells which selectively reabsorb the portions of the glomerular filtrate needed for normal electrolyte balance in the body fluids, it is undesirable, if it can be helped, to use excessive quantities of mercurial diuretics. It is probable that many of the electrolyte abnormalities which occur during the treatment of cardiac failure are the direct result of poor tubular function in the kidneys as a consequence of treatment with mercurial diuretics.

Summary

In this presentation it has been the purpose to present the various physiological readjustments of the body which occur when the heart becomes weak and fails to pump blood normally. Indeed, were it not for these physiological compensations, even slight failure of the heart would probably be lethal. The first physiological compensation following acute failure of the heart is increase in the autonomic reflexes which cause massive sympathetic discharges to the heart and to the peripheral vascular system. However, for a period of several days to several weeks following acute failure of the heart, fluid retention occurs, and this in turn increases the return of blood to the heart. This helps to correct the low cardiac output which is often the major effect of heart failure. Unfortunately, the retention of fluid by the circulatory system during the days following acute heart failure cause at the same time intensification of the symptoms of pulmonary congestion and peripheral congestion. Thus, though the cardiac output may return back toward normal, the congestive symptoms may be exacerbated. There are times when the increasing congestive symptoms, particularly pulmonary congestion, can cause death of the patient a week or more following acute failure of the heart.

Treatment of patients with cardiac failure is often paradoxical, for, as pointed out in the above discussion, patients with low cardiac output failure are occasionally greatly benefited by transfusion, whereas patients who have severe congestive heart failure are usually greatly benefited either by the actual removal of blood from the circulatory system or by other means of diminishing the circulating fluid volume.

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School of Medicine
University of Mississippi

Treatment of Syphilis

This summarization attempts to cover the essential information on the subject, including therapy, and is designed as a time-saving refresher for the busy practitioner.

Syphilis control and treatment has been possible, in any real sense, only for the past 40-50 years. The discovery of the *Treponema pallidum* by Schaudinn in 1905, the diagnostic tests of Wassermann, 1906, Neisser and Bruch, the perfection of Salvarsan by Ehrlich, 1910, were all milestones along the way. Since 1943 the antibiotics, especially penicillin, have revolutionized the treatment of syphilis.

It is most enlightening to delve into books on therapeusis in the 19th century and peruse the chapters on syphilitic treatment by way of contrast with present day methods. Eberle's Practice of Medicine, 1831,[1] preceded the Wassermann test by about 75 years. He states, " All agree that in genuine syphilis mercury is indispensable to the removal of the disease; but this forms but a small portion of the great number of venereal cases met with in practice and it is frequently almost impossible to determine from the external character of the disease whether it be true lues or only one of the various venereal affections which have been described. It will be sufficient to observe, where cutaneous and other secondary symptoms do not yield, in a reasonable time, to the use of sarsaparilla, compound decoction of woods, antimonials, rest, and an equable temperature and simple and uniritating diet, recourse should be had to a more or less active course of mercury; the moderate and gentle use of mercury will greatly expedite the malady"; "although very generally a mild mercurial influence, regularly sustained, will procure the benefits—yet instances occur where—after long mild mercurial action without benefit—then will yield to full salivation."

Clendenning in his Methods of Treatment, 1937,[2] gives an outline for the treatment of syphilis in all its stages in less than 5 pages and then the reader, under the methods of treatment (another 15-20 pages), is struck by the emphasis placed upon the frequent possibility of toxic reactions during the use of these heavy metals, i.e., vasomotor reaction with death, the visceral changes in liver and kidneys, etc. Clendenning stresses also the need for the preparation of the patient before each injection: checking the skin, testing the urine, how recently food was ingested or did elimination occur; is there evidence of salivation or bismuth line or abscess formation from last injection? "It will be seen that if the patient gets the amount of treatment outlined above he will be under intensive, almost continuous treatment for 1½ to 2 years."

In the present method of treatment, by contrast, more and more syphilologists have discarded the heavy metals and rely

on penicillin alone because of the favorable results, its safety, the shortened course of treatment [The Society for Investigative Dermatology Meeting in New York May 30-31, 1953, reported on a new repository penicillin containing DBED (dibenzylethylene-diamine penicillin G 600,000 units, procaine penicillin G 300,000 units and potassium penicillin G 300,000 units which in a single injection gives uniformly good results)] and the low cost of such treatment.

For a very complete survey of the recent literature on syphilis the reader is referred to the comprehensive articles by Beerman *et al.* in 1952[4] and 1953.[5] In preparation for this article, we have summarized these and many of the original papers.

Syphilis therapy, since the first use of penicillin in the army in 1944 and by civilians in 1946, has radically changed. Simplicity and ease of treatment, the shorter duration of treatment and fewer side effects have all contributed toward making the management of syphilis no longer the work of a few, mainly dermatologists, but of many, the general practitioners. For epidemiological purposes syphilis is really two diseases.[7]

1. *Early Syphilis*—during the first 2-4 years after acquirement. Infectiousness is largely concentrated in the first year and diminishes rapidly so that by the end of the fourth year, the risk of transmission from one adult to another has almost disappeared.

2. *Late Syphilis*—the duration since onset is more than 4 years. At this stage it is a public health problem comparable to the noninfectious diseases like cancer and hypertension.

In April, 1951 Curtis *et al.* in the *A.M.A. Journal*[8] in their article on Penicillin Treatment of Syphilis gave the following outline of Treatment Schedules with penicillin procaine in oil with aluminum monostearate.

For the small percentage of cases which show clinical relapse, a second complete course should be given as soon as clinical signs of relapse occur—another 5% who maintain positive serological tests but no signs of clinical relapse should be given the advantage of a second course but in very few will it result in serological reversal within a year's time.

In an Editorial in the *New England Journal of Medicine*[9] is stressed the importance of recognizing symptoms during the early hours after an initial dose of penicillin for gonorrhea which may call attention to the presence of unrecognized syphilis. These are febrile reaction with chilly sensations and headache beginning 4-6 hours after a single injection of 150,000 units of penicillin procaine. It is suggested that the physician inquire into the possible occurrence of these when the patient returns after his first injection of penicillin.

On the basis of the above results they concluded that schedule II was inferior to the others and not to be used; schedule IV was superior. They found the incidence of reinfection twice as high in primary as in secondary syphilis. The attainment of seronegativity with secondary syphilis at the end of one (1) year was as follows.

Schedule I—63.4%
Schedule II—55.9%
Schedule III—57.6%
Schedule IV—78.3%

In the summary of 1953, Beerman *et al.*[5] have collected further data on the use of the single or few dose schedules which vary greatly in their results. Rein[6] used a single injection of 1,200,000 units of P.A.M. (P.A.M. is crystalline procaine penicillin G gelled with 2% aluminum monostearate) and found it adequate for primary syphilis and a single dose of 2,400,000 units adequate for secondary syphilis. If 1,200,000 units were injected weekly for 2-4 weeks, the same results occurred.

Jones and Heyman,[7] on the other hand, found that single doses of 1,200,000 units

of P.A.M. caused a retreatment rate of better than 50% and retreatment rates in groups given 2-4 weekly injections were slightly higher than when given repository penicillin more frequently.

Parkhurst and Weinstein[11] found that adequate penicillin levels were obtained for 96 hours, after a single injection of 2,400,000 units and for 48 hours after each injection of 1,200,000 units in 100% of the patients. The results of this treatment compare favorably with results following the use of:

1. 2,400,000 units of aqueous penicillin G in 60 injections over 7½ days,
or 2. 4,800,000 units penicillin in peanut oil and beeswax in 8 injections over a period of 8 days.

Type of Syphilis		Dosage
EARLY		
Primary Secondary		2,400,000 units at first treatment (may be equally divided in both buttocks) followed by 4 injections at 4 day intervals of 600,000 units
LATENT		
LATE		
Osseous Cutaneous Visceral Mucous Membrane Cardiovascular (with no decompensation)		6,000,000 units as 600,000 units for 10 days or 600,000 twice weekly for 5 weeks
NEUROSYPHILIS		
All types		6,000,000 to 12,000,000 units as 600,000 units daily or twice weekly
PREGNANCY		
1st or 2nd Trimester		4,800,000 units 600,000 units twice weekly for 4 weeks or 1,200,000 units once a week for 4 weeks
3rd Trimester		600,000 units daily for 8 days
If labor is imminent		2,400,000 units at one time; repeat in 1 week if not delivered.
For relapse cases		900,000 units once a week for 4 weeks (3,600,000 units)
CONGENITAL		
Early — less than 2 years.		Either of three (3) schedules:
		1. 10,000 units per lb. of body weight daily for 10 days
	or	2. 15,000 units per lb. of body weight twice weekly for 4 weeks
	or	3. 40,000 units per lb. of body weight once weekly for 4 weeks
Late — more than 2 years		6,000,000 units 600,000 units daily or twice weekly
PROPHYLAXSIS		1,200,000 units in one treatment

These authors feel that a single injection is as effective as the others and exclusive of follow-up a single clinic visit can complete the treatment.

If these massive single or few dose schedules are subsequently found to be as effective as initial communications indicate, mass ambulatory treatment of early syphilis with practically no inconvenience is assured.

Latent Syphilis A diagnosis of latent syphilis" is made in patients who manifest no clinical signs of the disease, have positive serological tests and normal spinal fluid.

The aim in the treatment in these patients is to prevent the development of sequelae.

Penicillin has been found to be very effective for the benign forms of latent syphilis, i.e.: the cutaneous and hepatic. It is extremely difficult to evaluate the results of treatment but it has been found advisable to give at least one retreatment with fairly large amounts of penicillin for patients who continue to have relatively high titers on serological tests more than one year after their original treatment for probable early latent syphilis. Thomas, Landy *et al.* in their report,[12] used 3,500,000 units to 4,000,000 units given over 10-12 days with retreatment of 4 to 12 million units. In their series, 22% became seronegative after treatment and 21.3% had a drop in titer to less than 10.

Cardiovascular Syphilis Penicillin is a safe, effective base treatment in addition to the medical care of these patients, in the management of cardiovascular syphilis. The serious Herxheimer reactions so dreaded and frequently encountered with arsenicals are rarely found with penicillin therapy.

(The Jarisch-Herxheimer or Herxheimer reaction is a flare-up of the disease on the institution of treatment. The mechanism is a problem and probably in the nature of an immune response or even part of an allergic reaction. Its site, at least in part, is in the cellular tissues. In the heavy metal era it was controlled by two devices—1. initial very low dosage, and 2. the preliminary use, as "preparation," of the more slow acting heavy metals. It has been shown that the Herxheimer reaction with penicillin therapy is not related to dosage as in arsenical therapy.)

Stokes *et al.*[13] also were unable to recognize any unequivocal cases of therapeutic paradox with penicillin. The conception of therapeutic paradox was brought out by Wile in 1922. He stated that a person might be injured even fatally by the rapidly induced healing of a syphilitic lesion in a vital structure as the liver or heart which allowed no time for functional readjustment. With the heavy metals this was avoided by the same 2 devices as used in avoiding the Herxheimer reaction.

Sinclaire and Webster[14] conclude also that these two (2) reactions have been exaggerated and that preparatory heavy metal therapy does not prevent them and should therefore be dispensed with and that penicillin alone is the best treatment for cardiovascular syphilis.

Stokes *et al.*[13] advocated the following treatment: 1. Hospitalization, and 2. Round the clock schedule, every two hours with Crystalline Penicillin G (Sodium) 40-80,000 units for a total varying from 4,800,000 to 9,600,000. (Procaine penicillin may be given, 300,000 units twice daily or 600,000 units once daily to the same total dosage.)

Barnett and Small[15] concluded, from 334 cases studied, that penicillin treatment is effective when administered after cardiovascular disease has developed but before it has reached the symptom-producing stage. It is most effective before the diagnosis of C.V. disease has been established and as the disease advances into the later stages of heart failure it becomes less and less effective. The groups were divided into the 1. asymptomatic, 2. mild

symptom group (which had dyspnea or precordial pain but no objective myocardial insufficiency) and the 3. moderate and 4. severe with signs and symptoms of heart failure to a lesser or greater degree.

In trying to evaluate the results of therapy all are agreed that the reversal of the blood serological tests to negative is no longer felt to be the objective and it is frequently emphasized that almost one half of the patients with cardiovascular syphilis showed concomitant clinical or laboratory evidence of neurosyphilis.

Johnson and Shapiro,[4] as reported by Beerman, suggest that the best procedure in prognosticating the course for these patients is not the physical examination, the electrocardiogram or the x-ray but the orthodiagram. Changes in the orthodiagram, including the appearance of early aneurysm, increase in size of heart, dilation of right subclavian artery, warned that treatment had not arrested cardiac damage.

In summary:[1d, 4] 1. Penicillin can be given without fear of a severe reaction; neither therapeutic shock nor paradox was produced in C.V. cases. Deaths were largely explained on other grounds.

2. Penicillin is well tolerated by the decompensated heart, with clinical improvement in a high percentage of cases. Favorable response was obtained in some cases of paroxysmal tachycardia.

3. Anginal pain was relieved in four out of five cases.

4. Aortitis, uncomplicated, showed improvement in one third of the cases.

5. Aortitis with regurgitation—over one half showed improvement.

6. Aneurysm with symptoms carries a poor prognosis, but four out of five showed some improvement.

7. All patients experienced a sense of well being.

Neurosyphilis Neurosyphilis may be divided into two (2) categories

1. *Asymptomatic*—recognized by positive spinal fluid—without symptoms

2. *Symptomatic*

a. Inflammatory — acute syphilitic meningitis, meningovascular syphilis.

b. Degenerative — tabes, paresis, primary optic atrophy. (Treatment in this group, no matter what kind, heavy metal or antibiotic, can never restore the destroyed nerve cells).

Penicillin Treatment Schedules in Early Syphilis

Alexander Schoch and Mantooth[11]—report on clinical experience in 500 cases in the following 4 schedules.

SCHEDULE	RESULTS
I. Calcium penicillin in oil and wax 900,000 units Bismuth ethyl camphorate 3 cc. Mapharsen .05 - .06 gm. All at 1 clinic visit	1. Failure rate 12.3% 6.4% relapse 5.9% reinforced
II. Procaine penicillin G in oil with 2% aluminum monostearate 4 cc. (1,200,000 units) in one dose	2. Failure rate 20.2% 12.8% relapse 7.3% reinfected
III. Procaine Penicillin G in oil with 2% aluminum monostearate 4 cc. (1,200,000 units) per week for two doses	3. Failure rate 13% 6.5% relapse 6.5% reinfected
IV. Procaine Penicillin G in oil with 2% aluminum monostearate 4 cc. (1,200,000 units) per week for four doses	4. Failure rate 8.5% 2.5% relapse 6% reinfected

Dattner both in 1951[16] and again in 1952,[17] emphasized that serial spinal fluid examinations are the best guide and clinical response the worst guide to the effectiveness of treatment and activity of neurosyphilis. In a follow-up study after therapy, the changes in the abnormalities in the cerebrospinal fluid may precede the clinical findings. These changes must be quantitative to be of value in the early detection of progression. It is advised that spinal fluid studies be made repeatedly over many years. Dattner and Thomas[18] have stressed the importance of spinal fluid findings in therapy as follows: 1. If the cell count and protein are above normal, the spinal fluid is considered to be active, even if patient is asymptomatic clinically, and treatment should be prompt. 2. If the cell count and protein of spinal fluid become and remain normal as the result of treatment, even though the quantitative Wassermann reaction and colloidal gold curve remain fixed, the progress of the process in the C.N.S. has been arrested or rendered *inactive* (even if there has been no clinical improvement) and further treatment is considered to be useless. 3. If the cell count and protein of the spinal fluid do not become normal after treatment, or, if after a period of being normal, values again become abnormal, the patient should be retreated. 4. Prolonged inactivity of the spinal fluid after treatment (spinal fluid having been tested at 6 month intervals over several years) indicates "the infection has been cured". In these patients persistent psychotic manifestations (i.e., absence of clinical improvement) are not therapeutic failure but are due to destruction of the parenchyma of the brain or to a psychosis which may have been released by the syphilitic inflammation or been coincidental. Further antisyphilitic treatment will never help here but shock therapy may. 5. Relapse of neurosyphilis after effective antisyphilitic treatment rarely, if ever, occurs after two years.[16]

Webster,[18] on the other hand, feels that both clinical and spinal fluid findings are necessary in the evaluation of treatment as he has found "inactive" spinal fluids before treatment in the presence of evidence of clinical progression.

Penicillin Alone or Penicillin Plus? There is a general agreement that penicillin alone is the treatment of choice in all forms of asymptomatic neurosyphilis and in syphilitic meningitis or neurosyphilis manifested only by pupillary changes. Ford, Stokes *et al.*[3] according to Beerman, found that in asymptomatic syphilis penicillin alone was superior to other types of treatment and nothing was gained by the use of the heavy metals before, during or after. They advise a total dosage of approximately 10,000,000 units over a period of no less than 10 days in the form of aqueous penicillin G or delayed action penicillin.

Curtis *et al.*[8] found penicillin as the penicillin procaine in oil with aluminum monostearate "an adequate drug for the treatment of *all* types of neurosyphilis that have responded to the older methods of treatment". They advocate a course consisting of a total 6,000,000 to 12,000,000 units in ten (10) injections either daily or twice weekly.

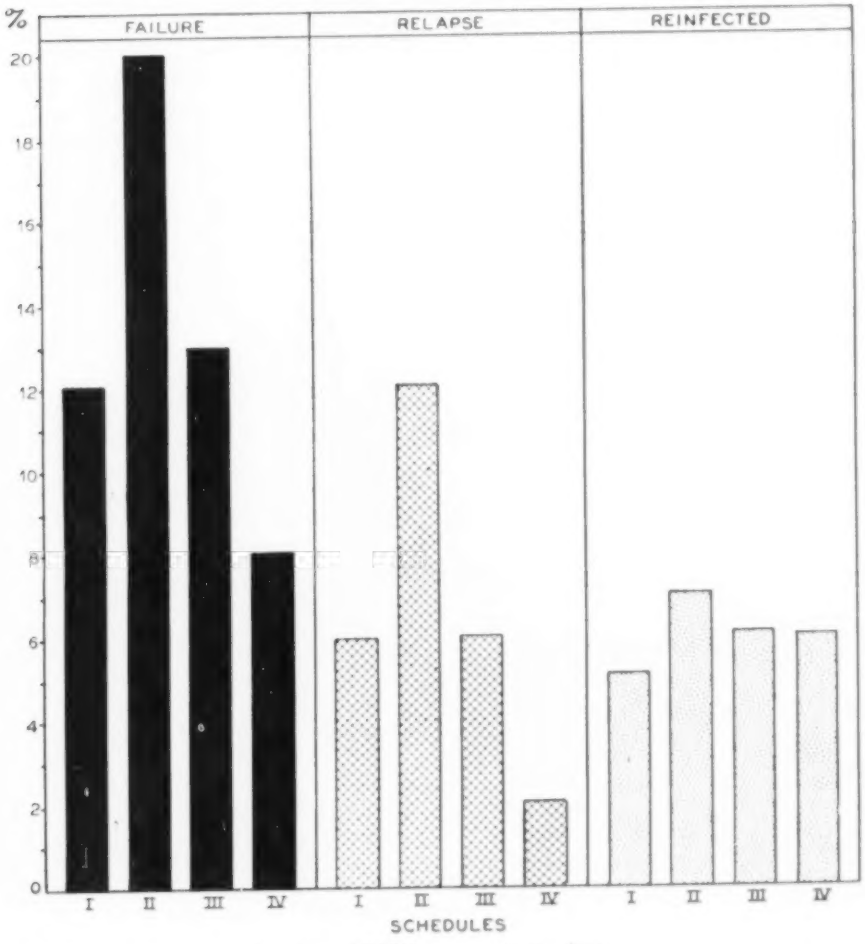
Ingraham, Stokes, *et al.*[19] also found penicillin adequate in all types of neurosyphilis with the spinal fluid response most rapid during the first year and reacting its maximum at the third to fourth year. The poorest, slowest response was in paresis and taboparesis and the greatest number of normal fluids in tabes dorsalis. Repetition of the course of penicillin resulted in very little improvement over the initial response when adequate dosage (5-10 million) was initially given. In comparison to metal chemotherapy and fever, the spinal fluid response is more rapid and reaches its maximum effect a year or two earlier.

The advocates of fever plus penicillin are fewer in Beerman's 1953 report[5] than

in 1952. They feel that the use of fever as malaria or hypotherm "blanket method" with the penicillin affords some additional clinical results in paresis whereas in tabes dorsalis both types seem adequate. Another group found that for the severe types of dementia paralytica found in state hospitals, penicillin combined with

GRAPH SHOWING RESULTS OF 4 PENICILLIN TREATMENT SCHEDULES IN EARLY SYPHILIS

BASED ON A REPORT MADE BY ALEXANDER, SCHOCH, AND MANTOOTH OF 500 CASES



I. Calcium penicillin in oil and wax 900,000 units.
Bismuth ethyl camphorate 3 cc.
Mapharsen .05 — .06 Gm.
All at one clinic visit.

II. Procaine penicillin G in oil with 2% aluminum monostearate 4 cc. (1,200,000 units) in one dose.

III. Procaine penicillin G in oil with 2% aluminum monostearate 4 cc. (1,200,000 units) per week for two doses.

IV. Procaine penicillin G in oil with 2% aluminum monostearate 4 cc. (1,200,000 units) per week for two doses.

malaria is the most desirable. Nicol and Whelan in Great Britain, as reported by Beerman, found that penicillin alone is adequate for neurosyphilis, that malaria plus penicillin is more adequate than malaria alone just as malaria plus heavy metals is better than malaria alone.

Fever therapy by "blanket method" as reported by Epstein and Allen[20] consisted of 4 or 5 episodes of fever with temperatures of 104-105° for five hours. They combined this with penicillin aluminum stearate 300,000 units daily for 20 injections, and found it particularly helpful in dementia paralytica, optic atrophy and meningo-vascular syphilis.

The use of the heavy metals with penicillin does not enter into Beerman's 1953[3] summary at all and in the 1952[4] summary, it is brought out that the advocates of penicillin plus (arsenical bismuth treatment), especially in France, feel that insufficient time has elapsed to properly evaluate penicillin as the average time between the appearance of the chancre and the first signs of tabes or dementia paralytica is 15-20 years.

Ocular Syphilis The treatment of interstitial keratitis with penicillin alone has been disappointing but the use of cortisone acetate locally in a 1:4 dilution of isotonic sodium chloride instilled locally—every hour 14 hours a day for 10 days and penicillin 600,000 units of P.A.M. for 12 days, has resulted in pronounced therapeutic response. Best results were found in early acute cases. There was prompt subjective relief, arrest of progression, and prevention of vascularization found in 11 cases by Crane and McPherson. Retreatment after relapse was found to bring a prompt response. This was found to be equally effective also in acute iridocyclitis due to syphilis and congenital interstitial keratitis.

Syphilis in Pregnancy Untreated early syphilis[23] resulted in a dead or diseased infant in 82% of cases as analyzed over a seven year period at the University of Pennsylvania and Philadelphia General Hospital. With treatment, 91-93% of the pregnancies resulted in the birth of a normal full term infant.

Penicillin is accepted as the most effective treatment for syphilis in pregnancy. Speiser[23] advocates the use of penicillin in oil with 2% aluminum monostearate (P.A.M.)

1. In early syphilis 1,200,000 units every other day for 4 injections.

2. In late syphilis 600,000 units daily for 10 injections or 1,200,000 units every other day for 5 doses.

3. In neurosyphilis 600,000 units daily for 15 days.

A successful result is signalled by a consistent fall in the titer of the quantitative serological tests. A rise in titer indicates relapse or new infection.

Curtis *et al.*[5]—use the P.A.M.—administered twice weekly as 600,000 units or 1,200,000 units once weekly for 4 weeks, a total of 4,800,000 (whenever possible in the first trimester of pregnancy). If syphilis is found in the latter stage of pregnancy, they use 600,000 units daily for 8 days or if labor is imminent, they suggest a single injection of 2,400,000 units to be repeated in 1 week if patient has not delivered. They aim their treatment primarily at the protection of the fetus and suggest it be used in the previously untreated or inadequately treated syphilitic pregnant woman. They state that therapy should be administered any time short of actual delivery. "Even if it appears to be too late to prevent infection in the fetus, penicillin therapy may be very effective in 'curing' such an infection in utero."

Godwin[25] states that the syphilitic women need not be retreated in every pregnancy. Treatment may be withheld, 1. if the mother previously received 4.0 gram of arsphenamine or its equivalent plus bismuth or at least 2,400,000 units aqueous or other equivalent penicillin, 2. if the mother shows no clinical signs of active

infection, 3. if the mother is seronegative or if seropositive is so in low titer (1:4). Such women (as Curtis[8] also stresses) should be kept under supervision with quantitative serological checks and retreated. If in doubt, it is safer to retreat. Curtis suggests 900,000 units P.A.M. once weekly for 4 weeks for this retreatment.

Congenital Syphilis Shaffer and Courville[26] emphasize that in the well treated mother a positive serological reaction on cord blood is not diagnostic of congenital syphilis. The babies of mothers treated late in pregnancy may show persistent but gradually decreasing titers which over several months will become negative. These latter are probably infants infected in utero but responding to a satisfactory degree to the treatment given to the mother.

Curtis *et al.*[8] state that if the syphilis is not discovered until the fifth month of pregancy, it may be too late to prevent infection of the fetus but not too late to cure it in utero.

Prognosis[8]—

1. In infants adequately treated before 6 months it compares well with acquired syphilis in primary or secondary stage.

2. In infants between 6 months and 2 years, it compares well with early latent stage.

3. Congenital syphilis of more than 2 years—exceedingly sero-resistant.

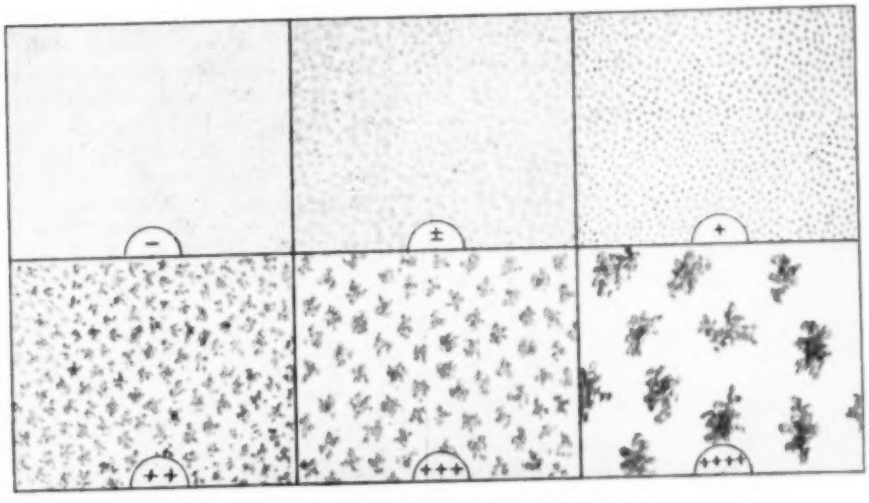
Caution is advised in the diagnosis of syphilis in new born infants in the absence of clinical signs of infantile congenital syphilis, for a positive blood test may be but a passive transfer of reagins from the mother (syphilotoxemia). These biologically false tests gradually change to negative in 2 to 12 weeks. If, on the other hand, the child has congenital syphilis, the serological tests become more strongly positive and clinical signs of infectious syphilis appear.

The following schedules[8] are suggested and are equally satisfactory—their use depending on the facilities available and the convenience to the mother.

Early Congenital (up to 2 years of age)

A. 10,000 units per pound of body weight of P.A.M. or aqueous penicillin daily for 10 days

B. 15,000 units per pound of body weight of P.A.M. twice weekly for 4 weeks



Reading of the Kline microflocculation test.

— Negative reaction ± Doubtful + Positive ++ Positive +++ Positive ++++ Positive

C. 40,000 units per pound of body weight once weekly for 4 weeks

Late Congenital (Past 2 years of age)

10 injections of 600,000 units of P.A.M. each for a total of 6,000,000 units at daily intervals or twice weekly for 5 weeks.

If neurosyphilis is present—treat it as late neurosyphilis.

For interstitial keratitis, Curtis advocates fever plus penicillin or the use of cortisone acetate as before discussed.

Reactions to Penicillin Kitchen *et al.*[27] report on their investigations into penicillin reactions and conclude that the incidence of reactions is falling primarily because of the increasing use of procaine penicillin. Others are not so optimistic and there is a constant search for newer hypoallergenic penicillin, inclusion of antihistaminic preparations with the penicillin, the efficacy of higher doses given in a shorter time and population desensitization tendency.

In the presence of scrotal and rectal pellagra following penicillin therapy, the use of 100 mg. of nicotinic acid three times daily for 12 days brought healing.[28]

Some of the other recently reported reactions are fatalities, nephritis or nephrosis, pseudoglycosuria, serum sickness-like syndrome, steatorrhea, laryngeal obstruction, periarteritis nodosa, erythema, multiforme, etc.

Feinberg & Feinberg in the May 9, 1953 *J.A.M.A.*[29] report on severe and fatal penicillin reactions and state they are occurring more and more frequently. They feel any type of penicillin by any route can cause this atopic or anaphylactic reaction. The majority of patients with anaphylactic reactions to penicillin have had previous injections or administrations of the drug although occasionally reactions follow with the first administration of the drug. Almost always there is an interval of weeks or longer between the non reacting and reacting dose, and usually previous and more moderate reactions precede the severe or fatal one. This type of atopic or anaphylactic reaction occurs more frequently in persons subject to other allergies but is *not* related to the hay fever or asthma produced by penicillin mold. The skin test for detecting sensitivity to penicillin, as suggested by the authors, is done by placing a drop of solution of crystalline penicillin (50,000-100,000 units per cc.) on a scratch or a speck of the powdered drug on a scratch and dissolving it with a drop of water or sodium chloride solution. A whealing, itching reaction occurs in 5 to 20 minutes. If the scratch test is negative and sensitivity is suspected, an intradermal test using .01 cc. of a solution of 100 units per cc. should be tried or, if only the intradermal test is used, the solution should contain only 10 units per cc.

Treatment of a reaction: at the first sign .5 to 1 cc. of epinephrine 1:1000 should be given intravenously and repeated in 2-3 minutes if no improvement. Follow this immediately with aminophylline 3.75 grains in 10 cc. intravenously. If cyanosis is present, oxygen should be given and if shock continues, plasma intravenously. They caution that penicillin not be given for trivial conditions because of the increasing frequency of reported reactions and that in their experience, there is a cross reaction between the various types of penicillin. When penicillin allergy was found of the anaphylactic type, penicillin O cross-reacted with penicillin G, therefore, a change over to the other type of penicillin made no difference. Another

Approved Tests

Five tests of serum or spinal fluid for syphilis approved by the U. S. Public Health Service as standard and recommended for use in all laboratories.

1. Kline test — microflocculation
2. Kahn test — microflocculation
3. Hinton test — flocculation
4. Eagle test — flocculation test best used with Eagle complement fixation test
5. Kolmer test — modification of the Wassermann complement fixation test

misconception stressed by them is that very infrequently was a skin test positive for procaine, which component of the penicillin has so frequently been blamed for the urticaria or dermatitis following penicillin.

Other Antibiotics in Syphilis

Terramycin This has only recently been tried out and there are few gross data available. Robinson and Robinson[30] treated their very small group with 48 grams, giving 3 gm. initially and .5 gm. every 4 hours for a total of 48 gm. in 15 days, orally administered. This is favored for safe mass treatment but has been so little used as to make evaluation difficult at this time.

Aureomycin Robinson and Robinson,[4] as reported by Beerman, found that surface treponema will disappear in 18 to 72 hours when Aureomycin is given either by mouth or intravenously and the lesions heal in 7 to 14 days. The titer of the serological reaction diminishes. No reaction was found after intravenous method (100 mg. once daily for 15 days or 200 mg. once daily for 15 days), but nausea and vomiting fairly severe in nature, were found in some with the use of the oral route (1 gram and 2 other doses of .5 gm. at four hour intervals for 15 days or 3 grams in a single dose followed by .5 gram every four hours for 15 days).

Another group, Olansky, Hogan *et al.*,[31] found that primary and secondary lesions healed as rapidly as with penicillin. Treatment failed in all patients treated for only one day and the greatest percentage of seronegative cases occurred where patients were treated with 60 mg. per kilogram of body weight a day for 8 days. They feel it is a therapeutic agent of particular value in neurosyphilis and cardiovascular syphilis because of the milder and less frequent Herxheimer reactions. Aureomycin's greatest value lies in patients sensitive to penicillin. In their 1952[5] report (Beerman's summary), they substantiate these findings and add the suggestion that patients getting either Aureomycin or chloramphenicol in this dosage: 60 mg. per kilogram of body weight for 8 days, for other diseases, need not be treated with penicillin for a concomitant syphilis.

Kierland and O'Leary used Aureomycin in neurosyphilis with good clinical and laboratory results. The total dosage of 50-75 grams was equivalent in effect to penicillin in the improvement of both the cell count and protein of the spinal fluid. The reactions included nausea and anorexia or even vomiting and diarrhea. They feel that Aureomycin by mouth is indicated in those patients with neurosyphilis who are sensitive to penicillin.

Chloramphenicol (Chloromycetin) The use and results, including the dosage of

	NEGATIVE	DOUBTFUL	POSITIVE
CONTROL	 Complete Lysis	 Complete Lysis	 Complete Lysis
TEST	 Complete Lysis	 Partial Lysis	 No Lysis

Reading of Eagle Complement-Fixation Test

this drug, closely parallel Aureomycin. The additional hazard lies in the toxicity of this drug for the hematopoietic system. Many cases of aplastic anemia have been reported with the use of chloramphenicol and it is advisable, therefore, to make repeated blood counts on patients receiving this drug for long periods.

Comment The clinical testimony left by our forefathers in medicine, but without statistical proof, attests to the fact that the characteristics of the disease—lues, have changed in the 450 years of its history.[7] From an often rapidly fatal infection, one of exquisite chronicity has evolved. Malignant destructive lesions of skin, mucous membranes and bones, have been replaced by less obvious and more serious cardiovascular and central nervous system involvement or almost clinical latency.

These observations suggest that a gradual process of adaptation has led to a decrease in the virulence of the parasite or an increase in the resistance of the host. Evidence also has been brought forward to show that the progressive improvement in the socio-economic conditions of Western civilization has contributed to a decrease in the incidence of syphilis.

In evaluating our present day treatment of syphilis with antibiotics, these things must be borne in mind. It is indeed too early, as the French have pointed out, to be certain of the end result of our present day methods. Suffice it to say that with our shorter treatment schedules, ease of administration and fewer side effects, physicians are finding better patient cooperation and, therefore, better laboratory response of the infection than ever before.

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Diagnosis of Coronary Pain

MANUEL GARDBERG, M.D.
New Orleans, La.

Patients who present themselves with intermittent pain in any of those areas of the body in which pain due to coronary disease may occur furnish the physician with the most trying diagnostic problems of everyday practice. It is here more than anywhere else in medicine that "experience is fallacious, judgment difficult". The physician is under the pressure of the responsibility to provide an answer to the anxious question in the patient's mind (frequently unexpressed) regarding the presence of heart disease. The physician knows that it is never possible to be absolutely certain that coronary disease is not present. He also knows that it is frequently difficult and at times impossible to prove that it is present. Early in his experience he finds that he approaches these cases with some misgivings. Even after many years of practice he frequently cannot feel sure of himself. This is a healthy though troublesome feeling and will be found in all physicians who are conscientious.

In an attempt to arrive at a diagnosis in these cases three methods are employed:

1. History
2. Electrocardiographic observations
3. Response to nitroglycerin

It is not to be implied that the physical examination and other studies are not to be carried out. Such omissions are never justified for the physical examination or x-ray studies may reveal evidence pointing to some other cause for the pain (aneurysm of the aorta, mediastinal tumor, diaphragmatic hernia, or gallbladder disease). However, these examinations do not bear upon the narrower subject of this discussion, i.e., the recognition of the presence of coronary insufficiency. Admittedly, this paper deals with only part of a diagnostic study, not the whole.

Of course, if the symptoms are typical, following closely the descriptions in the texts and the literature, the diagnosis is fairly certain. If the paroxysms are relieved promptly (within 4 minutes) by nitroglycerin there can be no doubt. Unfortunately, in the majority of these cases the symptoms do not follow the book. It is with this large group of "atypical" cases that this discussion is concerned.

The Electrocardiogram is very valuable in the solution of many of these problems but it is necessary that it be employed properly and that its limitations be recognized if we are to bring our errors to a minimum. Most frequently the electrocardiogram shows definite signs if the tracing is made during an attack. Between attacks it is apt to be normal. Even an abnormal electrocardiogram between attacks does not permit us to conclude that there is necessarily any relationship between the electrocardiographic abnormality and the patient's symptoms. Many older persons have abnormal tracings anyway, and their pains may be due

to diaphragmatic hernia, gallstones or arthritis of the spine. On the other hand, if the electrocardiogram made between attacks changes in a pathologic manner over a period of several days during which attacks are occurring it is possible to conclude that the pains result from coronary disease although no opportunity has been had to demonstrate electrocardiographic changes *during* an attack.

While the demonstration of typical electrocardiographic changes during an attack is the most pathognomonic sign obtainable a great deal of practical difficulty is encountered in attempting to make electrocardiograms during an attack. To do this one must arrange to dash to the patient's home with the apparatus upon a moment's notice. Frequent frustration by arrival after the attack is over and much expenditure of energy is involved. However, much has been learned in this manner. It was soon found, too, that an electrocardiogram made just after an attack frequently still showed diagnostic changes. If the attacks are occurring frequently it is easier to admit the patient to the hospital, place the apparatus at the bedside and await an attack. This has also been done in many cases, in the office.

Unfortunately, attacks of coronary insufficiency are occasionally not accompanied by electrocardiographic changes. In one case electrocardiograms made during five successive severe attacks were entirely normal. During the next attack marked changes were observed.

The difficulty encountered in obtaining observations during spontaneous attacks led to the employment of exercise to precipitate an attack and/or electrocardiographic evidence of coronary insufficiency. For eighteen years the author has employed twenty deep knee bends (fewer for older persons). This method has revealed many cases which would have otherwise been undetected. However, frequently exercise will not bring on an attack and will produce no electrocardiographic changes in persons who, a few days later, are found to have pronounced electrocardiographic changes during a spontaneous attack. A negative exercise test, then, means nothing. The value of the exercise test can be increased by making tracings five minutes after and ten minutes after the exercise as well as immediately after the exercise is completed for not infrequently the discomfort and/or electrocardiographic changes do not appear for some time. Only once in a great many tests has the author seen myocardial infarction follow this test. However, no patient has been asked to perform this test who has been having very frequent attacks of pain or whose resting electrocardiogram shows evidence of old infarction or of extensive myocardial disease. Some judgment must be exercised.

A great deal of help has been derived from reproducing in the office the conditions under which the attacks have occurred. If the patient states that attacks occur upon walking about after a meal or upon lying down after a meal he is permitted to have a meal brought to the office and is then asked to walk about the hall or to lie down (depending upon his history) and electrocardiograms are made whether attacks occur or not.

The ballistocardiogram is now under investigation in relation to this problem but has, thus far, not proven of great value. The greatest difficulty here resides in the fact that too many persons over forty years of age have abnormal ballistocardiograms which are unexplained. Also many persons with proved myocardial infarction and others with proved coronary insufficency have normal ballistocardiograms (by present standards).

Even after several weeks' observation one may fail to have the opportunity to make electrocardiographic observations during a spontaneous attack, one may fail to find electrocardiographic changes

during an attack if he has that opportunity, one may fail to be able to precipitate an attack by exercise or by reproducing the conditions during which, according to the history, they customarily occur, and no changes may be observed in the resting electrocardiogram. In many cases the attacks are too short to try nitroglycerin for diagnostic purposes. In spite of any or all these things including a normal ballistocardiogram the atacks may later be proven to be of coronary origin. Under these circumstances if the attacks are not "typical" both patient and physician find this uncertain state of affairs extremely trying. Anything which may aid in early diagnosis and thus shorten the period of anxiety is worth while considering. Anything which may avoid an erroneous conclusion either positive or negative must interest the physician. No new "test" is offered here which will resolve these problems without fail, but some observations will be made which may prove to be helpful. These observations relate to the descriptions of the attacks which have been given by patients whose symptoms have been proven by the above described methods to be due to coronary disease. No case of myocardial infarction is included.

It is of the utmost importance to realize that the published descriptions of the *symptomatology* of coronary insufficiency are extremely inadequate; they are too limited in every possible regard. It is safe to say that many cases of coronary insufficiency are missed because the physician is not even aware of the possibility because the symptoms are not classical. The following is a description of the symptoms of myocardial ischemia as they have been encountered in a fairly large experience which has been carefully controlled electrocardiographically.

The description of the attacks is divided into four sections: 1) quality of the discomfort, 2) duration of the attacks, 3) location of the discomfort, 4) circumstances under which the attacks occur.

The Quality of the discomfort varies somewhat. It may be described as a sensation of pressure, of constriction, of burning, a dull ache, numbness and tingling or a sharp pain. Any combination of these may occur. Numbness and tingling commonly precede any of the other sensations and may also follow them as the attack disappears. Anxiety, nausea, feeling like belching, sweating, and dizziness have also accompanied any of the above sensations during or following an attack. At times there is a feeling of weakness but rarely syncope although one case was seen in which syncope was the only symptom. Rarely is the discomfort described as being "sticking" in character.

The Duration of the attacks is extremely variable. They may last anywhere from eight seconds to more than an hour. Usually if pain is brought on by exertion its duration will depend upon whether the patient discontinues the exertion immediately or continues it. However, occasionally the pain disappears even though the exertion is continued. In most cases the duration of the pain varies between three and twenty minutes but the diagnosis of coronary insufficiency should not be missed because the attacks are "too short" or "too long". There is a tendency for the duration of attacks which do not accompany exertion to last the same length of time in the same patient.

The Location of The Discomfort and Its Radiation deserves the most careful study. It varies tremendously from patient to patient, but there is a marked tendency for the location of the pain and its radiation to remain the same in every attack in the same patient, although the *extent* of the radiation may vary with the severity and the duration which the attack achieves. The discomfort may begin in and remain confined to the upper, mid-, or lower sternal re-

gions or in the epigastric region. It may begin in and remain confined to the little finger of either hand or the little fingers of both hands, and the same applies to the wrists, forearms, elbows, arms, and shoulders. When it is in the shoulder the discomfort may be felt to be in the joint, anterior to it or posterior to it. In the rest of the upper extremity it may be described as being on the inner surface, deep, or on the outer surface, or all three. Frequently, discomfort in an extremity (or both extremities) tends to spread proximally during an attack, e.g., pain in the wrist spreads during the progress of an attack to the elbow, arm, shoulder, and, finally into the chest. In other cases the spread or radiation is in the reverse direction, pain beginning in the chest spreading progressively to the shoulder (or shoulders), arm, elbow, forearm, and finally to the wrist or little finger. If an attack is short either spontaneously or due to the administration of nitroglycerin the full extent of the spread or radiation is not attained, but the direction and order of the radiation rarely varies in the same patient. In its extension up or down an extremity the pain may skip any of these locations: e.g., beginning in the chest it may then be felt in the elbow, then in the forearm and finally, the wrist, skipping over the shoulder and the arm. Often when both extremities are involved the spread of the discomfort is symmetrical. However, one extremity, often the left, becomes uncomfortable before the other in many cases and if the attack does not last long enough the symmetry is not achieved. The location of the first discomfort in an attack and the direction and order of its radiation tends to remain remarkably constant in all attacks in the same patient.

The discomfort may begin in and remain confined to the throat, to the lower jaw, usually the left, or both jaws. It may begin in and remain confined to the ear, usually the left, or both ears. Again, it may begin in the throat and then spread up to the jaw or ear, or to the jaw and then to the ear. It may begin in the chest and spread to the throat and thence to the jaw and ear. In this spread it may skip regions as described for the extremities. Also, as was described for the extremities, it may begin in the more distal location (the ear) and reach the chest last.

The discomfort may be confined to the upper left pectoral area or to the lower left pectoral area. It may begin in and be confined to both upper or both lower pectoral areas. It may consist of a vice-like band of constriction about the whole chest, at either the upper or the lower levels. As in the other locations described it may begin on one side and spread to the opposite side, to the extremity areas, or to the head areas or to both, unilaterally or bilaterally.

The discomfort may begin in and remain confined to the interscapular area, or beginning here may penetrate the chest to reach the sternal areas and thence spread elsewhere. Again, the reverse direction of spread is common. It may begin in and remain confined to either or both scapular areas or suprascapular areas. Beginning here it spreads commonly to the extremity or extremities and is ascribed to bursitis or to arthritis of the spine. Occasionally from the scapular area it spreads to both the hypochondrium of the same side and to the shoulder.

It is clear from the above that the pain of coronary insufficiency may occur in almost any part of the upper half of the body, either primarily or as radiation. While recognition of this fact will at first seem to contribute confusion to the problem its acceptance will actually lead to more careful search in cases in which the diagnosis is often not even suspected and it will prevent us from too easily coming to the conclusion that the patient has a globus hystericus, neuralgia, bursitis, arthritis of the spine, gallbladder disease,

or a neurosis. Furthermore, as experience with the great variety of descriptions of pain accumulates certain patterns emerge to claim attention because they are encountered repeatedly. In addition to the classic description of pain in the chest with radiation to both arms or to the left arm, there is the pain in the throat or neck with spread to the jaws and ears. Seldom are *paroxysmal* attacks of pain following this pattern due to any disease other than coronary insufficiency. Another phenomenon worthy of notice is the manner of radiation of the pain during each attack which recurs in this experience with considerable regularity. Repeatedly a regular centripetal or centrifugal progression or spread of the pain is encountered which occurs in stages which may succeed one another with greater or less rapidity. The similarity to the spread of renal pain in stages to the right lower quadrant, the testicle and then the thigh is inescapable. *Paroxysms of pain occurring in the upper half of the body which always begin in the same area and always spread to the same areas in the same manner are most often due to coronary insufficiency.* This manifestation was not encountered in diaphragmatic hernia. It does occur in gallbladder disease (colic) for here the pain may begin either in the right shoulder, the right scapular area or the right hypochondrium and then radiate to the other areas in a regular manner in repeated attacks. Other areas may also be involved. One case was seen in which attacks due to coronary insufficiency (as evidenced by electrocardiographic changes and relief by nitroglycerin) and attacks due to gallstones (no electrocardiographic changes, no response to nitroglycerin, jaundice on the following day) were both producing pain which began in exactly the same area and radiating to the same areas in the same regular manner. There is no simple solution to such a problem. If the pain involves areas including the epigastrium, the right hypochondrium, the sternal areas or the right shoulder gallbladder disease should be considered. If advanced gallbladder disease is present, especially stones, the electrocardiogram made during attacks or as described above will have to solve the problem. If electrocardiographic changes are seen during an attack which are actually characteristic of coronary insufficiency then the patient *has* coronary insufficiency even though the attack is known to be a gallbladder colic (as evidenced by a palpable gallbladder during the attack or the occurrence of jaundice afterwards). It is fallacious to speak of such cases in any other terms—the patient has both diseases.

In spinal arthritis pain may begin in the same area and progress to other areas in a regular manner but the paroxysmal nature of the attacks is usually not too closely simulated except under certain circumstances which will be taken up later under another heading.

Actually the more bizarre the location of the point of origin and the areas of radiation of the pain the more likely are the paroxysms of the kind under discussion to prove to be of coronary origin. In one case pain began in the left shoulder and then spread to the circumoral area in every attack. There is no differential diagnosis in such a case as no other disease causes such attacks.

In spastic colitis pains in the chest, even over the manubrium, often occur which progress across the chest and often into the left arm, but here the pain moves rather than spreads. Spastic colitis gives more difficulty in diagnosis when it causes high chest pain which does not move. Again, in repeated attacks the point of beginning of the pain and the areas to which it moves are apt to change. In hysteria the symptoms are not constant from attack to attack.

The *circumstances under which the attacks of coronary insufficiency occur* vary in an almost unbelievable manner, but

here again, there is a tendency for a particular pattern to be characteristic for each individual. It is generally stated that the attacks frequently are precipitated by exertion. This is true but much qualification of this statement is badly needed. Some of the qualifications offered here are believed to be important diagnostically. Pain on walking one or two blocks is a frequent complaint. If the patient is questioned further on this point it would be expected to find that similar or much greater exertions of a kind other than walking also cause pain, but frequently an amazing incongruity is encountered. Many persons have pain on walking one half to one block and yet have no discomfort upon climbing long flights of stairs. Some state that they can climb stairs all day long without difficulty. This disproportionate effect of various kinds of exercise is seen so frequently that it is necessary to warn physicians not to be misled by such histories. Especially if the description of the discomfort is "atypical" the physician is apt to be led by this curious relationship of the attacks to exertion to conclude that the case is one of hysteria. Actually, the hysterical patient is apt to give a more "typical" history—the relationship of the attacks to the degree of exertion is apt to be more regular.

It is important to note that patients who complain of the regular production of pain on walking one block are frequently able to walk about the house all day without having attacks. Some have attacks every morning when walking to the street car to go to work but do not have them when taking the same walk on the way home in the evening.

The attacks often occur following meals, especially after large meals. Some persons have attacks after meals who do not have attacks after exertion and vice versa. The value of such histories in diagnosis is not very great. However, not too infrequently we find a patient who has no pain on eating and no pain on walking but who has pain if he walks after he eats. Frequently the patient does not put these things together but simply gives the history "that most often the pain occurs when he is walking back to the office after having his lunch." As a regularly recurring phenomenon this is not encountered in other conditions than coronary insufficiency.

Another frequent circumstance under which the pain occurs is the assumption of the horizontal position. An attack occurs just as the patient lies down to go to sleep. Usually the one attack occurs and when it is over the patient can lie down and go to sleep without difficulty. This symptomatology can be mimicked by spinal arthritis and the distinction is not easy except after several trials with nitroglycerin. Generally, if diaphragmatic hernia has been ruled out and the response to nitroglycerin is good no other condition need be considered. Some patients have no pain on lying down and no pain after eating but complain that they do have pain if they lie down immediately after eating. If the patient sits up for a half hour or so after eating he finds that he can then lie down without having discomfort. Also, after the pain has begun he can relieve it by sitting up. This history is virtually pathognomonic of coronary insufficiency, especially if diaphragmatic hernia has been ruled out. *Relief of the pain by emptying the stomach with a tube does not prove that the pain is not of coronary origin.* This has been done repeatedly during attacks which were proven to be attacks of coronary insufficiency. Some patients who have pain on lying down after eating are relieved by vomiting.

Emotional Tension, more especially sudden anger, very commonly precipitates attacks. This may be more pronounced after a meal than at other times. Continuing and unconscious tension undoubtedly increases the frequency of attacks and it seems almost certain that it ac-

counts for the frequent nocturnal attacks (nocturnal angina) which awaken some patients all night long. In many such patients it is not too difficult to prove that the attacks which awaken them from sleep occur at the climax of exciting dreams. These cases are easily distinguished from the decubitus cases by the fact that the latter are frequently relieved by sleeping in the sitting or inclined position.

Occasionally attacks are related to the sex act. In most of these the pain actually occurs before the act is begun and seems to be related more to excitement than to physical exertion. The importance of the sex act as a cause of attacks has been rather small in this experience.

The pattern may be pain on walking, pain on lying down or any one or combination of the circumstances just described, but in any single case there is here, again, a remarkable tendency for the pattern to be constant in the same patient.

Summary

The diagnosis of coronary insufficiency must rest either upon electrocardiographic evidence or upon the description of typical attacks aided by response to nitroglycerin (the latter being of no avail when the attacks are of short duration). An attempt has been made here to add to the list of typical descriptions of pain. Attention is especially drawn to the description of the locations of the pain and the circumstances under which they occur.

301 Medical Arts Building
3439 Prytania Street

Doctors Say Brodie Twin May Hope for Effective Life

The most coveted of all birthday presents — the prospect of a happy, effective life — was given to a two-year-old boy by four Chicago physicians.

The recipient was Rodney Dee Brodie. The donors were Drs. Herbert J. Grossman, Oscar Sugar, Paul W. Greeley and Max S. Sadove.

Rodney Dee probably will be able "to grow and develop as a happy, effective human being" despite his handicap, the doctors announced in a recent *Journal of the American Medical Association*.

"Rodney Dee can now sit alone, but cannot pull himself into a sitting position," the doctors stated. "He has good control of his head and good coordination of all extremities, and his jargon has increased in amount and in intelligibility. He is alert, responds to favored personnel, and makes attempts to feed himself.

"The hip flexors (which were tight, presumably owing to lack of standing) have become normal with physical therapy. It is difficult to assess the degree of development in all spheres because of the many factors, biological, traumatic and psychological, that have affected his state.

"There is still no solid protection for the brain, and the solution of this problem is now under active consideration. We are reluctant to use any foreign material over such a large surface of dura mater and under skin flaps, because of the hazards accompanying buried foreign bodies. Autogenous bone grafts appear to offer the best replacement for the calvarium that never developed, but the extensiveness of the defect makes accomplishment of closure by this means difficult.

"All the professional and technical skills have basically one objective — to permit this baby to grow and develop as a happy, effective human being. His handicap—like other handicaps—need not prevent him from fulfilling this goal."

The doctors are associated with the University of Illinois College of Medicine.

Surgical Treatment Of Mitral Stenosis

FORRESTER RAINE, M.D.*
Milwaukee, Wisconsin

Mitral stenosis, in its healed state, is a mechanical difficulty and, as such, its treatment by surgery has been envisioned for many years. The practical solution to the problem, however, has only been attained in recent years.

Mitral stenosis develops as a result of rheumatic heart disease. As the active valvular disease subsides, healing takes place. The mode and result of this healing depends on where the worst of the disease was as far as the valve leaves are concerned. If they are along the edge of the leaves and there was a good deal of destruction of the leaves themselves, healing will result in curling and shortening of the valve leaves, shortening of the involved chordae tendineae and a mitral regurgitation. If the primary amount of the disease was on the edges of the valve leaves without a great deal of leaf destruction, then the leaves tend to heal to each other at each commissure, narrowing the opening and producing mitral stenosis. The exact mechanism of the development of calcified valve leaves and valve ring and base is not known. The resulting mechanical effect, in mitral stenosis, produces the following changes in normal circulation. The flow of blood from the left atrium through the narrowed mitral orifice is slow. As a result, pressure builds up and distention occurs in the left atrium. There is back pressure into the pulmonary veins and increased capillary pressure in the pulmonary arterial bed. This, in turn, requires greater pressure in the pulmonary artery to force blood through this pulmonary bed and, as a result, there is increased pulmonary artery pressure. This, in turn, requires greater effort on the part of the right ventricle to force blood through the pulmonary artery and, as a result, pressures in the right ventricle increase and the right ventricle, to maintain this increased pressure, hypertrophies. In fully compensated mitral stenosis, then, there is hypertrophy of the right ventricle, increased pressure in the pulmonary artery, in the capillary bed of the lung, in the pulmonary veins and in the left atrium with enlargement of the heart due to the enlargement of the right ventricle and left atrium. Sufficient blood gets through the stenosed valve to maintain systemic circulation and the patient gets along satisfactorily under reasonable degrees of activity. This heart, however, is overworking constantly and the time comes when increased capillary pressure in the lung has gone on to capillary and arteriolar fibrosis with marked increase in the resistance to the flow of blood through the pulmonary bed. The heart becomes fatigued, the lungs are congested, hemoptysis occurs and pulmonary edema and right heart failure are the consequences. Activities must become greatly restricted. When the rheumatic heart has been over-

* Clinical Professor of Surgery, Marquette University School of Medicine, Milwaukee, Wisconsin.

worked for some time with the atrial dilatation, auricular fibrillation commonly occurs. These patients require digitalis for maintenance of ventricular rate and frequently diuretics for fluid elimination.

Symptoms produced by these circulatory changes will, in many instances, indicate the time and need for operative correction without actual pressures within the heart being determined by cardiac catheterization. Patients who have been able to do normal activities but have not been able to participate in strenuous activity gradually develop dyspnea when walking on level ground. They may begin to have hemoptysis. As pulmonary congestion increases, they require two, three or four pillows for sleep. Any unusual exertion will throw them into pulmonary edema. Nocturnal dyspnea will occur with increasing frequency. These patients, as they have relatively pure mitral stenosis, are now candidates for sugical intervention.

For the purpose of selection of patients for operation and the appraisal of results, a rather commonly used system of grading has been done.

GRADE 1—Patients with murmurs indicative of mitral stenosis but no symptoms.

GRADE 2—Patients with mitral stenosis whose disease is stationary and whose activities, though restricted, are not becoming more limited.

GRADE 3—Patients who are progressively getting worse in that their activities must be more and more restricted.

GRADE 4—Those with probably irreversible damage to heart and lungs who are rapidly going downhill.

From this grading it will be seen that the selection of patients will usually be from Group 3. The salvage from the Grade 4 group can be considerable, as is seen in our one excellent and three good results out of six, but is going to carry a considerable mortality rate and the ultimate degree of recovery cannot be entirely satisfactory. As time passes and experience increases, probably a much larger percentage of the Grade 2 group should be operated upon because then the heart damage which has occurred by the time they reach Grade 3 may quite possibly be prevented.

The Operative Technique has been quite well standardized throughout the country with contributions from many different individuals. The salient points are as follows: The left chest is entered either anteriorly or posterolaterally through the fifth interspace or the bed of the fifth rib. The pericardium is opened widely and a heavy pursestring is placed about the base of the auricular appendage which is clamped. The appendage is opened widely enough to admit a finger. As the clamp is opened, the finger is inserted into the left atrium. The degree of stenosis and regurgitation is estimated by the finger. The two commissures are then split by finger pressure if it can be done (which it can in about 85 percent of the cases). The remaining ones must be cut with a knife of some type which is slid along or attached to the finger. Damage must not be done to the valve leaves, the splitting or cutting being done only in the commissure so that regurgitation does not increase over that found preoperatively. In fact, in many instances, because the valve leaves are released, regurgitation will be less after opening the valve than it was before. When the valve has been opened to its base at the end of each commissure, which should permit the admission of at least two fingers, the finger is withdrawn, the pursestring tied tightly, excess appendage cut away and the appendage itself closed with silk or cotton sutures. The pericardium is closed loosely so that tamponade could not occur and the chest is closed airtight with an expanded lung.

The incidence of embolic phenomena occurring at the time of operation is con-

siderable. This results from dislodgement of thrombi in the auricular appendage or the atrium or the breaking off of calcified plaques when the commissures are fractured. Many means of attempting to prevent this have been devised, the most common being occlusion of the innominate during the operative procedure with temporary occlusion of the left carotid at the moment of valve fracture. Timing must be accurate here if one is to prevent cerebral damage from too prolonged occlusion to cerebral circulation. This, of course, does not prevent peripheral emboli from lodging. Thrombi in the auricular appendage can, of course, be removed before the finger is passed and these should not present a problem. However, attachments to this thrombus could extend beyond the appendage and might be dislodged when the base of the appendage is clamped.

Postoperative Care presents only a few specific problems. I always use an airtight intercostal drainage tube into the pleural cavity for 48 hours as a safety measure. This is attached to underwater drainage. Some degree of pericarditis nearly always develops which causes a substernal sense of tightness which is distressing to patients for a matter of four or five days. Patients who have had normal sinus rhythm prior to operation

RESULTS

	NO.	EXCELLENT	GOOD	FAIR	POOR	DIED	COMPLICATIONS
GRADE 3	22	12	7	1		2	6
GRADE 4	6	1	3			2	2

COMPLICATIONS: Emboli or Thrombus

(1) Hemiplegia: leg clearing, speech returned, arm only slight motion after 3 months.

(1) Speech center: normal speech after 6 months.

(1) Hemiopia: permanent.

(1) Left arm paralysis: recovery one week.

RHYTHM: Normal sinus to auricular fibrillation

(1) Converted in one day to normal.

(1) Converted in six days to normal.

(2) Remained in auricular fibrillation.

DEATHS:

GRADE 3

(1) Expired 3 days—never regained consciousness. No cause found at autopsy.

(1) Cardiac arrest when nasal catheter inserted for oxygen therapy 20 minutes postoperatively.

GRADE 4

(1) Expired 2 months. Staphylococcus septicemia with thrombi in left ventricle. None on mitral valve

(1) Expired one hour—cardiac failure.

may go into auricular fibrillation at the time of operation but in my experience are more likely to do it on the second or third day postoperatively. This can either be controlled at the time by quinidine or the rate of fibrillation can be controlled by digitalis and they can be converted to normal rhythm later by quinidine. Patients who have been fibrillating prior to operation seldom convert to a normal rhythm and their rate is controlled by digitalis postoperatively. Oxygen is administered routinely for the first two or three days and ambulation is started on the second or third day. Most patients leave the hospital on the eighth to tenth day, gradually increasing their activities over a period of a month.

The results of operation have been tabulated as follows:

Excellent—the patient thinks he is entirely well. They can do all normal activity without dyspnea, without palpitation and no longer need diuretics.

Good—Activities are greatly increased over their pre-operative status. They can walk good distances on the level, can climb at least one flight of stairs without any dyspnea but do have some real restriction in activity.

Fair—There is only moderate improvement over their preoperative condition as far as the degree of activity is concerned.

Poor—There has been no change.

A comparison of the results obtained in those with calcified valves and in those in whom there was no calcification reveals considerably better end results in those without calcification since they can have and do have a valve which functions quite satisfactorily. A calcified valve ring and leaflets cannot be too efficient and although there are some good results in the calcified group, the percentage of excellent and good results is less than in the uncalcified group.

The accompanying table, although comprising a rather small number of patients, will give some idea of the mortality rate and also the results which can be expected in the surgical treatment of mitral stenosis.

Two patients were explored who had no stenosis but pure mitral regurgitation. Their condition remained unchanged postoperatively. One of them eventually died of her regurgitation. One patient has been operated upon too recently to judge the results.

Conclusions

Properly selected patients with mitral stenosis can achieve a high rate of excellent and good results following mitral commissurotomy. If Grade IV patients in desperate condition are not accepted for operation, the mortality rate should be within reasonable figures. Most of the mortality here occurred in the earlier patients and the one who died of cardiac failure was virtually moribund at the time of operation. Emboli are bound to occur but by central nervous system protection can be held to a reasonable minimum without too serious consequences. Cardiac catherization confirms the diagnosis but is not absolutely essential when the patient is a clear cut tight mitral stenosis.

425 East Wisconsin Avenue.

The Use of Large Doses of an Antihistamine In Severe Allergic Crises

In Severe Allergic Crises

ROBERT J. ANTOS, M.D.
Phoenix, Ariz.

The following four cases are presented to show the experiences in giving very large doses of an antihistamine. Following the dictum of giving enough of a drug to get an effect, I have found that in these allergic crises the dose of the drug required is very much higher than the recommended dose. In this series of cases I used thenylpyramine,* of which the recommended parenteral dose is ten to twenty milligrams with a maximum of forty milligrams.

Case 1. May 1950. A thirty-six-year-old male Indian farm laborer was brought to my office by his employer; he was in obvious respiratory distress. It was found that he had been burning green oleander prunings and had inhaled much of the smoke. He began to cough and gradually got to the point of falling to the ground. He was brought to my office in the back of a pick-up truck. When seen, he was cyanotic, comatose, and blowing froth from both the mouth and nostrils. Oxygen was applied by face mask at six liters per minute. I gave an intravenous infusion of five percent glucose in water with 9 cc. of thenylpyramine solution (20 mg./cc.) added. This means 180 mg. of thenylpyramine was added to 1000 cc. of diluent, or 18 mg. to each 100 cc. According to the manufacturer, 20 mg. is the top dose. This was run at about 80 to 100 drops per minute and oxygen was given continuously. As soon as this was going, I went to get some epinephrine, and while doing so, the patient roused and began breathing more easily. I was torn between the desire to give the epinephrine or to wait and see what the thenylpyramine would do intravenously. Since his color was good and he was breathing better, I decided not to give the epinephrine.

After about 500 cc. of the solution had run in, the patient roused; this contained 90 mg. of thenylpyramine. His breathing was easy and the oxygen mask was removed. Auscultation revealed many mixed rales in both lung fields, so the I.V. was allowed to run slowly (50 to 60 drops per minute). When 900 cc. (162 mg.) had been given, his chest was clear and he said he felt fine. He left the office under his own power about two and three-quarters hours after treatment was started.

Case 2. February 1951. The patient was a thirty-seven-year-old white pharmacist who was in status asthmaticus. He had been taking epinephrine and all the other usual drugs for the past five or six days. On this day he was unable to reach his

* Histadyl (Lilly).

regular attending physician. His wife called me and when I saw him he was in a severe status asthmaticus. He had taken all the other medications without effect. I gave ½ cc. 1:1000 epinephrine subcutaneously and waited, but I waited in vain. Nothing happened. I thought of the thenylpyramine solution.

Not having an I.V. set-up, I began giving 1 cc. I.V. every five minutes until the patient said he began to feel "fuzzy." By this time I had given 7 cc. (140 mg.). I listened to his chest and was surprised to find that it was not so noisy. I was going to stop there, but the patient asked for another "shot", so I gave an additional 1 cc. I.V. (total 160 mg.) following which I gave 0.3 cc. 1:1000 epinephrine subcutaneously. Half an hour before, the epinephrine had had no effect; after the thenylpyramine was given it took effect immediately and the patient lay back and breathed easily for the first time in over a week.

Case 3. January 1951. This patient was a thirty-eight-year-old white housewife, para I, who had been plagued with asthma since childhood. She had been giving herself epinephrine subcutaneously for many years. I was called out to see her one afternoon and found her in severe status. I gave her aminophylline I.V. and she promptly fainted. Naturally I stopped this and hospitalized her. Immediately upon admission, an I.V. was started, consisting of 200 mg. thenylpyramine in 1000 cc. of five percent glucose in water. After 700 cc. had run in (in 65 minutes), she said she felt "far away." At this time it was noticed that her chest was clearing, so the rate of drip was slowed down from over 100 drops per minute to 50 to 60 drops per minute. An additional 100 cc. was run in when she complained of getting dizzy, so the infusion was discontinued. She had received a total of 800 cc. or 160 mg. thenylpyramine I.V. in about one and three-fourths hours. Following this, she was given 0.3 cc. 1:1000 epinephrine subcutaneously, and in about a minute she sank back on the pillow mumbling, "This is wonderful," and she fell into a much-needed sleep.

Case 4. May 1953. The same patient as Case 3. She had had mild flare-ups of asthma during the intervening two and one-half years, but nothing serious enough to worry her. A few days prior to the time I saw her, she had been doing some yard work, after which she burned oleander prunings and Bermuda grass clippings; the smoke of either is a strong allergic irritant. After twenty-four hours of intractable asthma over which epinephrine had no effect, her husband brought her to my office for "one of those big bottles." I requested hospitalization, as it could be seen that she was about as far into a status asthmaticus as one could be, but they both insisted on "the bottle first." We put 200 mg. thenylpyramine into 1000 cc. five percent glucose solution and started the I.V. After 550 cc. (110 mg. thenylpyramine) had run in, the patient said she was beginning "to feel it." The rate of flow was slowed from 100 drops a minute to about 50 drops a minute. After 275 cc. more had run in, she said she was getting dizzy, so the infusion was stopped. She had received 145 mg. thenylpyramine I.V. in two hours. Following this she was given 0.3 cc. 1:1000 epinephrine. Within one minute she breathed easily, sat up, and asked to go home.

After Cases 2 and 3 had recovered from their acute episodes, rechecks were made as follows:

Case 2. Three months after being without symptoms, but taking 50 mg. cortisone daily, this patient volunteered to take I.V. thenylpyramine to the point of being "fuzzy." Fifty mg. of the drug (2½ cc.) was diluted to 25 cc. and given slowly I.V. The "fuzziness" was noted after 30 mg. had been given. This refers to persistent "fuzziness" and not the peculiar sensation noted temporarily when the

drug, or any drug, is given I.V. too rapidly.

Case 3. This patient likewise was given the drug I.V. slowly, four and one-half months after her illness, during which time she had been well except for minor nocturnal bronchospasm. This patient noted the "feeling of saturation" after 22 mg. had been given.

These observations convinced me of the difference in dosages that must be given during acute allergic crises. I then gave I.V. thenylpyramine to a group of five known asthmatics who were not having asthma, and the doses given to reach the "feeling of saturation" were 22 mg., 26 mg., 36 mg., and 18 mg., and 18 mg. Then, when the next dust storm blew up and they developed asthma, the test was repeated and the doses given were 42 mg., 38 mg., 50 mg., 64 mg., and 48 mg. These five patients, plus Cases 2 and 3, are depicted in the following table:

The percent of increase is not in proportion to the clinical severity of the disease, but I believe that this small series illustrates the fact that in some of these cases of acute allergic crises we are not using high enough doses of the drug to get the desired effect. Although this series is small, it is hoped that it will be conclusive enough to stimulate further studies in the use of a dose "big enough to give effect."

Discussion It is my theory that during periods of allergic stress the amount of antigen, or whatever you want to call the histamine-like substance, is very high in blood and tissues. Small doses of antihistamine produce no appreciable effect because it is quickly absorbed or combined with whatever allergic offender is present in the tissues or blood stream. Not until all the excess of this antigen is neutralized or combined with some antihistamine, can the latter go ot work. When the concentration gets above a certain point, and when the antigen is neutralized, then, and only then, does the antihistamine have any ability to squelch allergic reactions.

In asthma it usually is quite high, but in status asthmaticus and pulmonary edema the amount of antigen is enormously high, and tremendously large doses of antihistamine are needed to neutralize it.

The median lethal dose (LD_{50}) of thenylpyramine for mice is 20 mg./kg. by vein and 182 mg./kg. by mouth. The I.V. LD_{50} is not known for man. If it were comparable to the above figure for

THENYLPYRAMINE DOSE NEEDED TO REACH "SATURATION"

	Normally	During allergic crises	Increase
CASE 2	30 mg.	140 mg.	110 mg. or 333 %
CASE 3	22 mg.	160 mg.	138 mg. or 627 %
CASE 4	22 mg.	145 mg.	123 mg. or 559 %
Other five cases:			
A	22 mg.	42 mg.	20 mg. or 90 %
B	26 mg.	38 mg.	12 mg. or 46 %
C	36 mg.	50 mg.	14 mg. or 40 %
D	18 mg.	64 mg.	46 mg. or 255 %
E	18 mg.	48 mg.	30 mg. or 166 %

mice, the LD_{50} for a 70 kg. man would be 1400 mg. of thenylpyramine given I.V. Thus the dosages used in this study were approximately 10% or less of the LD_{50}. In other words, the doses used were far below the median lethal dose of the drug, yet they were much higher than those commonly used clinically today. Many writers have written that antihistamines are ineffective in asthma. I believe the reason is simply a case of insufficient dosage.

Conclusion

Large doses of antihistamine, doses that under ordinary conditions are toxic, or even fatal, are required in some of these allergic crises. In this report are represented four cases which received large doses of antihistamine. The doses given were 162 mg., 180 mg., 160 mg., and 145 mg. Large doses of antihistamines are not fatal and are not convulsants in people with allergic crises. Whereas these doses are toxic under more normal conditions, they are life-saving during the crisis. A further small series of five cases is presented to show a less striking, though similar, result.

Although in one case I gave the antihistamine in divided I.V. doses, it is recommended that it be added to an intravenous infusion and given at approximately 100 drops per minute. When the allergic substance in the patient's blood begins to be neutralized, the patient usually will complain of being "fuzzy", "distant", or "dizzy." When this point is reached, usually after one hour, the infusion is slowed to 50 drops per minute and the patient reexamined, because shortly after this point is reached the patient will begin to clear and *then* there is danger of giving a toxic dose.

Except for the work done on animals, there are no other published works on this problem. All the animal experiments in determining fatal doses of the drug were done on normal animals. It is presumed the LD_{50} would be considerably higher if the animals were in an allergic state. Although the doses used here are much higher than those used clinically now, they are 10% or less of the LD_{50} of normal mice.

References

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20 West Riverside Street

Dermatophytid Treated With Cortisone

WILLIAM SAUNDERS, M.D.
Watertown, N. Y

Three cases of vesicular dermatophytid were recently treated with oral cortisone. The results were so dramatic, and this disorder is so commonly encountered, that it seemed a good idea to bring this to the attention of others.

The first case was that of a 49-year-old male employed in the manufacture of cheese. He had a past history of stomach ulcer which responded well to medical therapy. The present history was that for one month he had had vesicles and scales on the sole of the right foot. Four days before his initial visit a vesicular eruption had appeared on both palms and soles. A few vesicles also appeared on the dorsal aspects of the hands shortly thereafter. He was told to take oral cortisone in divided doses for a total of 200 mg. in the first 24 hours. This was to be repeated in the second 24 hours, and then 150 mg. daily in divided doses was to be continued for the next 48 hours. When he was seen, after four days of therapy, no vesicles were apparent on the hands. The vesicles on the left foot had all dried up. On the right foot the same situation existed except on the volar surface of the second toe where some vesicles were still visible in diminished size. The patient reported that he had taken only 8 tablets (25 mg. each) daily for two days. He then discontinued them because they bothered his stomach.

The second case was that of a 56-year-old female, wife of a physician. For one month she had had an eruption of the soles diagnosed as "athlete's foot." About one week prior to the first visit, a spread of the vesicular eruption of the feet was noticed, accompanied by the appearance of a vesicular eruption of the hands with itching. She was given symptomatic treatment along with cortisone, in doses of 25 mg. orally every 3 hours for a total of 8 tablets daily the first two days and one tablet every 4 hours on the third day after which she was told to return. Two days after the treatment was begun she telephoned to say that her hands and feet were "all well" and that she did not appear to need any further treatment.

The third case was that of a 2-year-old child with a *Tinea kerion* and *Tinea circinata* of a couple of weeks duration. A few days before the initial visit by the presenting physician, a diffuse, generalized eruption had appeared on the trunk and extremities consisting of tiny follicular vesicles. Examination showed a boggy area of the right parietal region of the scalp, 5 cm. in diameter. There was a smaller, similar eruption of the upper occipital region. On the helix of the right ear, and on the middle of the back, there were identical, scaly, erythematous patches of slightly less than one cm. in diameter.

He was getting Terramycin for a questionable pyelitis with fever. He was given local treatment to the scalp and to the eruption of the ear and mid back. On the second day that he was seen the eruption of the trunk appeared to be slightly worse, so cortisone was ordered. He was given 150 mg. orally in divided doses of 25 mg. each on the first day, thereafter 25 mg. less each day for a total of 6 days treatment. On the third day the generalized vesicular eruption had disappeared except for a few residual erythematous macules of the upper arms. These disappeared a couple of days later. The tinea lesions were slowly improving, unaffected by the cortisone.

Laboratory Procedures included direct microscopic examination for fungi. Ringworm type fungi were seen in the roofs of vesicles taken from the soles of both the first two cases, while lesions from the hands did not reveal fungi. Cultures were not made. In the third case, direct microscopic examination of hair from the involved areas of the scalp showed chains of large, ectothrix spores. On culture these were found to be *Trichophyton gypseum*. Blood count and urine examination in the third case were essentially normal.

Diagnosis in each of the first two cases was dermatophytosis with vesicular dermatophytid. In the last case, diagnosis was *Tinea kerion* of the scalp, *Tinea circinata* and vesicular, generalized dermatophytid consecutive to the *Tinea kerion*.

Summary

Such dramatic response to oral cortisone is worthy of note: In the first two cases almost complete clearing of the vesicular dermatophytid (without apparently affecting the basic fungus infection) followed two days oral cortisone with a total of sixteen 25 mg. tablets. In the third case the dematophytid was almost completely gone after three days oral cortisone using a total of fifteen 25 mg. tablets (following this the dosage was rapidly diminished over a period of three more days).

531-535 Woolworth Building

Clinico-Pathological Conference

New York University-Bellevue Medical Center Post Graduate Medical School, Department Of Medicine at Bellevue Hospital, Fourth Medical (N. Y. U.) Division

PATIENT L. S.

This was the 5th B.H. admission of a 63-year-old widowed Negro female. She was readmitted from home care in state of massive anasarca.

1st B.H. Admission was to O.B. Service in 1937. Records lost.

2nd B.H. Admission (9/12/51 to 9/20/51).

On admission, she complained of high blood pressure for 10-15 years, SOB for 2 years, SOB with gasping for 6 months and swelling of legs for 6 weeks.

P.I. Patient noted progressive dyspnea for 2 years until she was unable to climb 1 flight of stairs; 6 months PTA, she noted onset of PND which progressed until it awoke her 2-3 x nightly for past 6 weeks. Could not sleep flat; 6 weeks PTA, noted swelling legs and abdomen. Nausea and vomiting present for several weeks PTA.

Past History 40 years previously, she had swelling of legs with pregnancy.

For 10-15 years has had asymptomatic hypertension. Nocturia 1 to 2 x.

Px: *T 100, P 100, R 20, BP 215/125.*
T 100, P 100, R 20, BP 215/125.

Patient was a well-nourished, well-developed, obese Negro female obviously dyspneic with dependent edema. There were brown macules over body in patches. Arcus senilis. Fundi had some AV nicking and tortuosity of vessels only. Bilateral medium moist rales heard. Heart enlarged with grade II short apical murmur. $A_2 > B_2 \cdot 3+$ edema legs with poor peripheral pulses.

Course in Hospital Patient responded to digitalization and was discharged to clinic on 9th day.

3rd B.H. admission (5/29/52 to 7/9/52).

P.I. Patient had been followed in cardiac clinic since previous admission. She had been taking digitalis and weekly Mercuhydrin injections. In spite of this, pre-tibial edema recurred 4-5 weeks PTA and progressed. She also believed abdomen became swollen. Dyspnea increased and she was re-admitted.

Px: *BP 210/120, P 88, R 18, T 98.6.*
Other findings as on previous admission.

Course in Hospital Work-up revealed uremia and congestive heart failure. She was given Ca gluconate 1.5 gms. daily, Amphojel 15 cc. 3xday, K citrate 1 gm. daily with milk, digitalis leaf 0.1 gm. daily, and Na lactate 20 cc's twice daily with good clinical response. Her uremia and acidosis subsided and CHF improved. She was discharged to O.P.D.

4th B.H. Admission 7/30/52 to 8/8/52).

Laboratory Data

Urine

Date	Cath.	Color	S.G.	pH	Alb.	Sug.	Wbc.	Rbc.	Other
9/13/51	no	yell.	1.012	6.5	tr	0	0	0	Ca(PO4) crystals
6/2/52	no	pale	1.008	alk.	4+/600 mg.	1+	8-10	1-2	
Between 6/5/52 and 7/8/52, many urines with S.G. of 1.010 or less, 4+ alb. and loaded with wbc's.									
7/31/52	no	straw	1.018	alk.	4+/800	1+	many	2-3	
9/24/52	0	bloody	1.011	alk	4+	1+	loaded	many	

Blood

Date	Hgb.	rbc.	wbc.	Tr	P	L	M	E	B	ESR	Hct
9/19/51	14.5	4.50	5,550	3	80	15	0	2	0		
6/2/52	12.0	4.20	9,950	20	59	16	1	3	0		
6/10/52	10.0	2.85	10,450	9	58	24	2	7	0	65	29
7/31/52	10.5	3.20	7,800	6	51	34	3	6	0	61	33
9/19/52	8.0	2.72	12,250	4	65	24	1	6	0	72	24
9/26/52	10.5	3.42	12,000	5	67	22	2	4	0	59	33

Blood Chemistries

Date	Sugar	NPN	CO2	A/G	Chol. Esters	I.I.	CFT	Alk. P'tse	PUN
6/4/52	77	99	5 meq.	1.4/3.6	383/273	6	neg.	7.2	over 70
6/23/52			13.0	1.9/2.3					94
8/1/52			14.5		374/272				
9/15/52		112	8.0	1.9/2.0	410		neg.		
9/26/52	103		7.2						

Blood Electrolytes, etc.

Date	Na	K	Ca	P	Cl	Creatinine	BUN
6/4/52	142	3.9	5.9	7.2	116		
6/23/52	140	3.6	6.0	3.3			
8/1/52	137	4.5				7.1	
9/15/52	139	5.3			123	9.3	56
9/26/52	132	4.9			134	10.3	

During the intervening 3 weeks since discharge, patient noted progressive recurrence of generalized edema with slight weakness. Dyspnea had not recurred. She became unable to attend clinic and was re-admitted to be evaluated for home care.

Px: *BP 190/80, T 99, R 18, P 100.*

Findings were as on previous admis-

sions except that lungs were clear in spite of generalized anasarca including ascites.

Couse in Hospital On bed rest, low salt diet and digitalis, the edema subsided. On 4th day, herpes zoster was diagnosed by dermatologist because of vesicular rash on erythematous base with pain over left thigh. She was given a course of radiation and Aureomycin for this with good response. She was discharged to home care on 11th day on Amphojel, K citrate, calcium gluconate and digitalis.

5th B.H. admission (9/19/52 to 10/4/52).

While on home care for one month, the patient's edema again recurred and she was readmitted because of this and abnormal electrolytes. Dyspnea was not a prominent feature.

Px: *T 99.0, P 88, BP 140/80, R 24.*

Examination was as on previous admission except that anasarca was even more marked and included even neck and arms as well as abdomen, legs and back. Fluid was present over lower 2/3rds of both lung fields.

Course in Hospital Patient was obviously in uremia with passage of only 300-600 cc. urine o.d. Breath was acidotic. 1000 cc. whole blood was given for anemia on 7th hospital day. Temperatures fell to 94-95° by 15th day. Plans were made for giving either radioactive iodine to deaccelerate the uremia or to give her human albumin. Before either could be done, she quietly expired on 16th day.

Miscellaneous Mazzini negative on each admission.

Stool guaiac negative on each admission except 9/25/52 when it was 1+.

EKG showed left ventricular hypertrophy.

X-rays merely confirmed clinical enlargement of heart and congestive changes in lungs although the latter were usually not outstanding.

No urinary cultures were ever reported to have been taken.

Case presented from the wards of the Fourth Medical Division, Bellevue Hospital, Dr. Charles Wilkinson, Dir.

Write your own clinical impression or formulation here, if you wish.

Pathological Findings

This is an extraordinary instance of *nephrotic syndrome* since the kidneys had none of the anatomical lesions recognized to cause this picture. Instead there were severe *arteriolar nephrosclerosis* and some inflammatory changes suggesting chronic pyelonephritis. While we cannot be certain of it, we are inclined to regard the former as the dominant feature. There is no suggestion of chronic glomerulonephritis, amyloidosis or intercapillary glomerulosclerosis. There is no agreement among pathologists whether this type of nephrosclerosis has a pyelonephritis background—we doubt that there is such.

The present case must be regarded as a rare, if not unique, one.

There is almost no atherosclerosis of the major vessels, and only focal, mild cardiac hypertrophy—this in the face of protracted hypertension and terminal hypercholesterolemia. The thyroid was normal grossly; unfortunately, sections of it were not available.

A small area of lobular pneumonia with abscess formation was an incidental finding in the right lower lobe. A mild degree of hemorrhagic cystitis also was present.

PATIENT C. S.

This was the first B.H. admission (10/9/52) of C.S., an 80-year-old white male, retired, a widower and an egg inspector all his life before retirement 8 years previously. He entered complaining of back pain and inability to walk for 2 days PTA.

P.I. Patient stated that his general health had always been excellent except "arthritis" for 15-20 years.

Five days PTA Patient developed slight dull headache in back of neck but he was otherwise well and continued to be ambulatory.

Two days PTA He awoke early in morning with moderately severe pain over lumbar spine without radiation. The neck pain continued and neck became stiff. He was unable to get out of bed because of "shakes" and the back pain. Movement of legs was difficult. For the next two days, he remained alone in bed in his Bowery hotel room without food, drink or aid. A local physician was called and sent patient to the hospital.

F.H. and *S.H.* non-contributory. *P.H.* reveals that he had scrotal mass for 25 years.

Px *T-101.4, R-24, P-112, BP-105/55.*

Patient was a fairly well-developed, thin, white male who appeared toxic, lethargic and in moderate distress. He was lying flat in bed and was alert and cooperative. Occasional shaking chills.

Skin Skin was dry, inelastic and filthy. Increased pigmentation was present over both lower extremities. No petechial hemorrhages.

Nodes No striking adenopathy.

Head Dried blood over superficial bruise in left parietal region.

Eyes: Right pupil > left but both react L and A. Prominence of eyes with lid lag. A petechial hemorrhage was present in conjunctiva. Fundi showed "A.S. changes". Purulent conjunctivitis was present.

E.N.T. Mouth dry and parched. Palate and pharynx markedly reddened. Teeth in poor repair. Buccal mucosa suspicious for petechial hemorrhages.

Neck Thyroid not enlarged. Marked nuchal rigidity with pain on flexion of head on chest.

Chest Emphysematous. Moderate dyspnea. Few dry rales left base, otherwise clear to P & A.

Heart PMI 6th ICS, 3 cm. left MCL, NSR. VR-PR-90 $A_2 > P_2$ • Soft apical blowing systolic murmur.

Abdomen Poorly relaxed but without tenderness. A firm, non-tender spleen was palpated 2 fbths. below left C.M. No other organs or masses were palpable.

Genitalia A large mass which transilluminated was present in left testicle. The mass was inflamed.

Rectal No masses. Prostate soft and not enlarged. Stool guaiac negative.

Extremities There were marked deformities, stiffness and changes of chronic arthritis in all extremities but most marked in hands which showed bilateral ulnar deviation. In addition, there was acute tenderness, redness, swelling of carpal-metarcarpal joints and of right index finger and left middle finger. Bilateral varicosities were present in both lower extremities.

Neurological DTR's were present and within normal limits. Absent abdominals and cremasterics. No Babinskis. Bilateral positive Kernigs and Brudzinskis. Generalized weakness. Marked tremors of hands and fasciculations of leg muscles.

Hospital Course Spinal tap revealed 3+ Pandy, a few fresh rbc's, gram + cocci and normal manometrics. Patient was placed on 4 million units penicillin which was increased to 10 million u. o.d. within first 24 hours hospitalization. In addition, he was started on sulfadiazine and streptomycin. Later on first hospital day, Aureomycin was also added to therapy. By third day, temperature was normal

but rose on each subsequent day to 99.4 or 99.6.

A G.U. consultant believed the scrotal inflammation was a cellulitis over a hydrocele. On the 7th day smears and cultures of nose, throat, blood and joint aspirates were all positive for *Straph-aureus;* coagulase positive. This organism was sensitive moderately to penicillin and streptomycin but more sensitive to Aureomycin, Terramycin and Chloromycetin. Penicillin and streptomycin were cut and Aureomycin and sulfadiazine continued.

On 8th day, patient was doing poorly. Because of a CO_2 of 10 meq/L, 500 cc. M/6 Na lactate + 500 cc. normal saline was given i.v. with re-institution of 10 million units of penicillin o.d. Patient expired quietly on 9th day (10/17/52).

Laboratory Data

Urine

Date	Cath.	Color	Sp.G.	pH	Alb.	Sugar	Wbc	rbc.	other
10/10/52	no	Cldy.	1.011	ac.	1+	0	3-6	10/20	hyaline & gran casts
10/14/52	yes	Cldy.	QNS	ac.	tr.	1+	2-4	0	hyaline casts
10/16/52	no	Cldy.	1.011	ac.	1+/5C	1+	0	loaded	

Blood

Date	Hgb	rbc	wbc	tr	P	L	M	E	ESR	Hct	Smear
10/10/52	12.0	4.47	11,100	35	56	4	3		55	35%	4 histiocytes seen
10/15/52	11.5	3.60	21,650	26	59	3	1	2	57	35%	toxic granules retics 8%
10/16/52	11.5	2.57	25,900						57	35%	clumping of rbc's.

Blood Chemistries

Date	CO2	Creatinine	Na	K	Stool blood	Mazzini
10/10/52	10 meq	2.7			neg	neg
10/16/52		3.3	124	6.0		

Spinal Taps

Date	I.P.	F.P.	Character	Pandy	Cells	Prot.	Sugar	Cl	Wass.
10/9/52	90	40	?	3+	few rbc's	81	74	124	neg.
10/10/52	120	64	clear	2+	150 rbc's	108		123	

(Spinal fluid cultures negative)

Miscellaneaus E.K.G. 10/14/52 Auricular fibrillation with left BBB; probable old posterior wall myocardial infarction.

X-Rays None.

Case presented from the wards of the Fourth Medical Division, Bellevue Hospital, Dr. Charles Wilkinson, Dir.

Write your own clinical impression or formulation here, if you wish.

Pathological Findings

The source of the staphylococcic bacteremia proved to be *acute bacterial endocarditis* of the aortic and mitral valves. Septic embolism took place in the left ventricle as well as in several of the metocarpo-phalangeal joints. Such secondary pyogenic complication of *rheumatoid arthritis* has been seen here recently in another case of bacterial endocarditis (Acc. #40038). There was no underlying rheumatic involvement of the heart. The staphylococcus could not be recovered by culture at necropsy; this was the result of treatment with the antibiotics.[1] Minor inflammatory and regenerative changes were found in the glomeruli and convoluted tubules of the kidney. Some of these were the result of the circulation of staphylococcal toxin,[2] others were frankly embolic. For want of a better name, this has been classified as acute glomerulitis.

Minute infiltrates of lymphocytes were found in the endoneurium of the brachial plexus and sympathetic chain. These have been regarded by some as specific lesions of rheumatoid arthritis[3]—a conclusion that probably is not warranted.

There was some degranulation of the basophilic cells of the pars intermedia of the pituitary. This lesion is similar to that seen in the pituitary in Addison's disease and has been described as a lesion of rheumatoid arthritis by A. G. E. Pearse.[4]

An incidental finding is *acute ulceration of the esophagus with formation of intranuclear inclusion bodies.* This was first described by J. Pearce[5] and has been observed in only a few additional instances.[6] The inclusion bodies are of Cowdey's Type A and the appearance of the lesion suggests that it is due to herpes simplex. Although no labial involvement was present in this patient, oropharyngeal herpes has been demonstrated recently in a number of instances in which stomatitis was lacking.[7]

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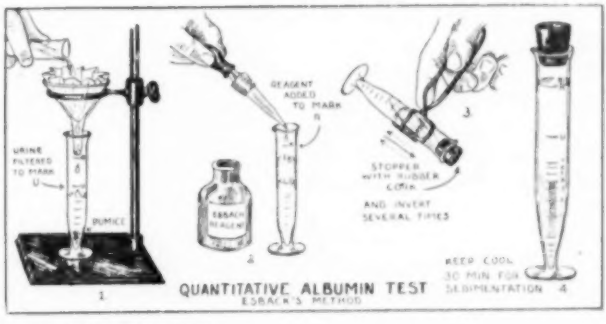
Clini-Clipping



QUANTITATIVE ALBUMIN TEST
ESBACH'S METHOD

Shoulder Injuries

Part Two

Dislocation of the Shoulder

Dislocations of the shoulder (gleno-humeral joint) comprise about forty to sixty percent of all dislocations. They occur in patients of all ages, but are most common in athletic individuals in the third decade of life. The usual causes are: a. a fall on the abducted arm without hyperabduction, b. a direct blow to the head of the humerus from behind, c. hyperextension of the abducted arm, d. excessive external rotation in abduction, and e. hyperabduction (causing inferior dislocation). In all of these injuries the head of the humerus ruptures through the inferior portion of the joint capsule and out of the shallow glenoid fossa, and comes to lie anteriorly (sub-coracoid dislocation) (Figure 10), antero-superiorly (subclavicular dislocation), inferiorly (subglenoid dislocation), or posteriorly. The sub-coracoid dislocation is the commonest; the sub-glenoid is next in frequency.

Examination of the patient with a dislocation of the shoulder reveals the following (Figure 11): a. There is loss of the rounded contour of the shoulder; b. the patient keeps the elbow flexed and the forearm internally rotated, and supports the forearm and elbow with the other hand, keeping the arm abducted at about 25 to 30 degrees; c. there is resistance to movement of the arm in any direction because of severe pain in the region of the shoulder. b. In the case of the common anterior dislocation, the head of the humerus is palpated as a rounded mass under the coracoid process. X-rays confirm the diagnosis, and should always be taken before and after reduction to determine position and the possible presence of an associated fracture of the glenoid or humerus, which is a common complication, especially in older patients.

Treatment consists of prompt reduction under anesthesia. To attempt reduction without the relaxation afforded by general anesthesia is to cause the patient considerable discomfort, make the reduction more difficult for the operator, and increase the likelihood of tearing the soft tissues and/or fracturing the humeral head or the glenoid rim. The minimal amount of force should be used. The safest method of reduction is direct traction (Figure 12). With the patient lying on his back, counter-traction is applied to the chest by an assistant. The operator flexes the elbow and makes firm steady pull on the injured arm in line with the slightly abducted humerus. The humeral head will be felt to slip over the glenoid rim, and back into the glenoid fossa.

Placing a foot in the axilla to provide counter-traction (the Hippocratic method) risks injury to the axillary structures, and is unnecessary. The Kocher maneuver, advocated for the reduction of sub-coracoid dislocations since the early nineteenth century, is at last being recognized as a dangerous procedure, to be used only when the direct traction method fails to effect

reduction in old cases. Its danger lies in the risk of fracture of the humeral shaft, injury to the circumflex nerve, and avulsion of the rotator cuff. The maneuver consists of three steps (to be carried out under general anesthesia): a. external rotation of the flexed forearm, b. adduction of the arm, by forcing the elbow across the front of the chest, and c. internal rotation of the forearm, placing the hand upon the opposite shoulder. The dislocation is usually reduced during the second step in the procedure. A long-standing dislocation is ofter very difficult to reduce because of the changes in the soft-tissues which render them inelastic. If two or three attempts at closed reduction are unsuccessful, open reduction should be considered to prevent further soft-tissue damage.

In young patients (under 30), the danger of a "frozen shoulder" is slight, but the danger of recurrent dislocation is great. These patients should be treated by immobilization for four to six weeks after reduction. This can be accomplished by means of a sling and swathe, or an adhesive Velpeau dressing (Figure 13). If the latter is used, felt pads should be placed in the axilla and under the elbow, and the hand should be left entirely free for exercises.

In older patients (over 45), the danger of "frozen shoulder" is great, but the danger of recurrence is small. A patient in this age group should be given a sling for four or five weeks, but active "gravity-free" exercise should be started immediately (Figure 14). (Twice a day the arm is removed from the sling, and the patient bends over at the waist and swings the shoulder through as wide a range of motion as possible, being careful, however, not to externally rotate the forearm.)

Complications of acute dislocation of the shoulder are: a. Injury to the brachial plexus or axillary vein. (This requires immediate reduction, and consultation with an orthopedic surgeon is advisable.) b. Injury to the axillary circumflex nerve with resultant atrophy of the deltoid muscle. (This is often a complication of over-strenuous attempts at reduction.) c. Fracture of the glenoid or humerus. (Discussed below) (As a general rule the dislocation should be reduced first, then the fracture treated.) d. Recurrent dislocations. (Common in young individuals, and requiring operative repair to prevent repetition. Acute recurrences can be treated as described above.)

Fractures and Fracture-Dislocations of the Upper Humerus These injuries usually result from falls on the outstretched arm. The type of fracture depends upon the severity of the force, the direction of rotation of the shaft of the humerus during the fall, and the age of the patient. In the very young, the injury usually results in dislocation or epiphyseal separation; in the second and third decades of life, in dislocation; and in older patients, fracture-dislocation.

Fracture of the Surgical Neck of the Humerus Fractures of the surgical neck of the humerus are common, and their management is dependent upon their impaction and position:

a. *Fragments impacted in good position in young active adults, or impacted in good or poor position in the aged* (Figure 15): No reduction is necessary. A collar-and-cuff (Neck-wrist sling) can be used for support (Figure 16). After the first twenty-four or forty-eight hours, daily gravity-free exercises should be started. After two weeks, anti-gravity exercises (finger-ladder, shoulder wheel, etc.) are begun, and by the end of six to eight weeks, healing and restoration of function should be complete.

b. *Minimal displacement in young patients:* No reduction is necessary. A collar-and-cuff should be worn with no motion allowed for three weeks, after which gravity-free exercises can be started, and the further treatment is the same as

that described above for impacted fractures.

c. *Marked displacement:* (Figure 17) The pectoralis major tends to pull the lower fragment into the axilla, and the supraspinatus abducts the upper fragment. Reduction should be performed under general anesthesia, and is usually best obtained by traction on the arm (with the elbow flexed) in the direction towards the midline of the patient's body, and manipulation of the fragments into position. After reduction is obtained, the fragments can be impacted by upward pressure on the flexed forearm; after this, the treatment is the same as for impacted fractures. Attempts at reduction of the fractures by abduction usually result in increasing the deformity. If it is impossible to obtain reduction by traction, consultation with an orthopedist is advisable to determine the advisability of open reduction, or closed reduction by means of overhead traction with a wire through the olecranon.

Fracture-Dislocations Involving the Greater Tuberosity Fractures of the greater tuberosity of the humerus are fairly common in association with shoulder dislocations. If the tuberosity follows the head of the humerus into its dislocated position, or if it occupies its normal position in relation to the glenoid, usually no treatment is needed other than reduction of the dislocation, and subsequent management like an uncomplicated dislocation, disregarding the fracture. If two attempts at reduction of the dislocation are unsuccessful, a complication can usually be assumed to exist, most commonly displacement of the biceps tendon from its groove, into a position between the two fragments. This complication, of course, requires open reduction. A fracture-dislocation in which the greater tuberosity is displaced upward under the acromion (Figure 18) requires prompt open reduction with internal fixation of the tuberosity. Abduction splints are useless in this case.

Fracture-dislocation in which the lesser tuberosity is avulsed (by the subscapularis) require only reduction of the dislocation if the displacement is slight, but open reduction is indicated if after reduction of the shoulder, the tuberosity still is not in its normal position.

Rupture of the Rotator Cuff The term "rotator cuff" is used to designate the muscles which fuse with the joint capsule about one-half inch from its distal margin: the external rotators (supraspinatus, infraspinatus, and teres minor) which attach to the greater tuberosity, and an internal rotator (subcapularis) which attaches to the lesser tuberosity. These muscles rotate the humerus and provide stabilization of the joint.

Ruptures of the cuff, particularly the supraspinatus tendon, occur fairly commonly in patients past middle life, in whom there are degenerative changes in the tendons of these muscles. The rupture of the cuff may be incomplete (consisting of a partial tear through the supraspinatus tendon), complete (a tear completely across the tendon), or massive (detachment of a large part of the cuff). The characteristic clinical picture is that of a middle-aged person who after a fall had sudden severe pain in the shoulder and inability to abduct the arm, and whose x-ray is negative for fracture, dislocation, or calcium deposit. The arm can be passively abducted, but when released, falls to the side. If procaine infiltration of the region of the supraspinatus tendon permits movement (because of release of muscle spasm), but the arm cannot be held in 90 degrees of abduction against resistance, the cuff is ruptured. In late cases, seen long after injury, there is pain and weakness of the shoulder, and atrophy of the supraspinatus and infraspinatus muscles.

Treatment of partial rupture, in which the power is not totally lost, is physiotherapy, consisting of heat, massage, and

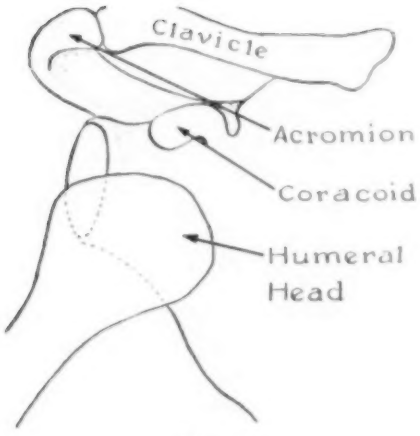


Fig 10

Subcoracoid dislocation of right shoulder.

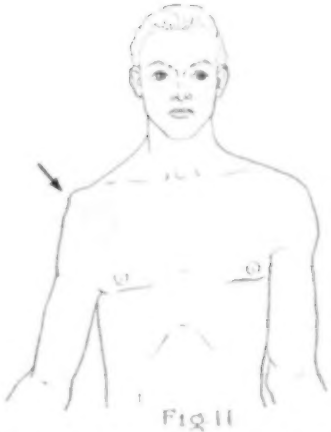


Fig 11

Characteristic deformity in patient with subcoracoid dislocation of right shoulder. (Note the prominence of the humeral head.)

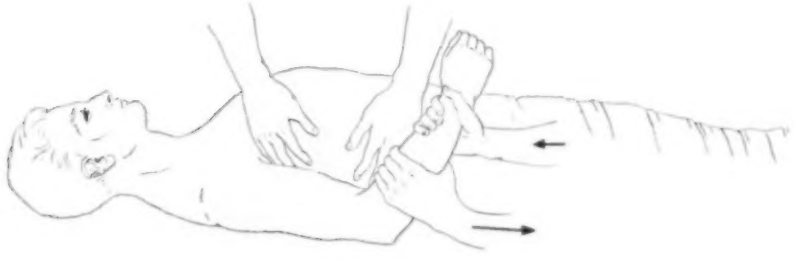


Fig 12.

Reduction of dislocation of shoulder by direct traction.

Fig 13

Adhesive tape Velpeau dressing.

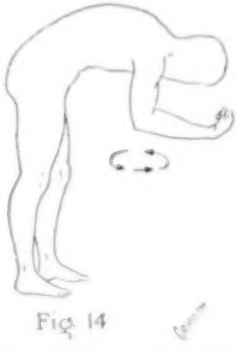


Fig 14

Gravity-free rotatory shoulder exercise.

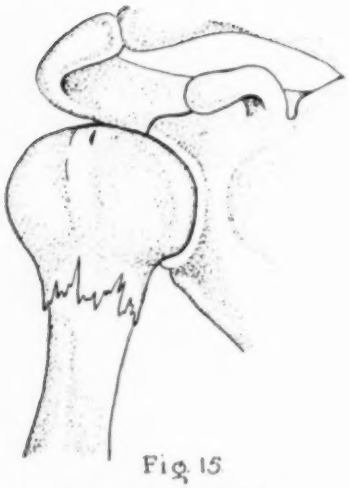
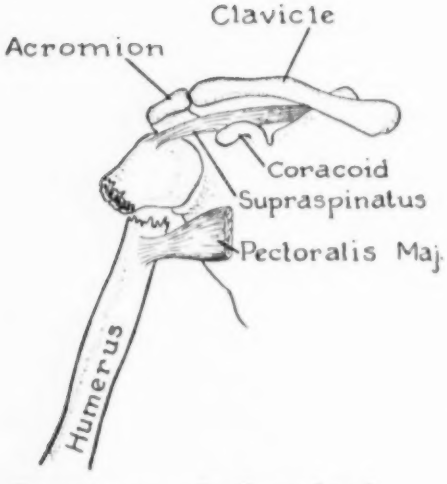


Fig 15

Impacted fracture of surgical neck of humerus (in excellent position).

Fig 16

"Collar-and-cuff" sling.



Fracture of Surgical Neck with Displacement

Fig 17

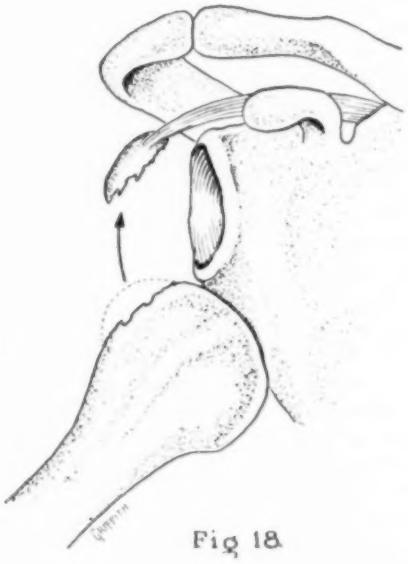


Fig 18

Sub-glenoid dislocation of shoulder with associated avulsion fracture of greater tuberosity of humerus.

active exercise, for three to six weeks, until pain in gone and function is normal. In the treatment of complete ruptures, some surgeons advise immediate operative exploration and suture. Others recommend conservative therapy as for partial ruptures. Since the disability is considerable in the case of an untreated rupture of the cuff, consultation by an orthopedist is advisable.

Cardiac Women Now Can Bear Children with Greater Safety

Women with heart disease now can bear children with greater safety and expectations of success than ever before, in the opinion of Dr. James A. Brussel, Queens Village, N. Y.

However, cardiac women should know the risks involved in pregnancy complicated by heart disease, he wrote in a recent *Today's Health* magazine.

"Perhaps the most difficult question any physician has to answer is that put to him by a woman with heart disease who asks if it is safe for her to have a baby," Dr. Brussel stated. "No single answer will apply to the thousands of such prospective mothers.

"Each case must be considered individually. Every factor — domestic as well as clinical — must be carefully weighed. No two problems are the same. After the doctor has made his diagnosis and informed the patient of the risks involved, the final decision must rest with the patient and her husband."

Heart disease complicates from one to three per cent of all pregnancies. Ninety per cent of such complications is attributable to rheumatic fever; the remaining ten per cent includes high blood pressure, congenital cardiac defects, and syphilis. The death rate from heart disease complicating pregnancy would be even higher, he added, if statistics included women whose deaths occurred up to two years after childbirth rather than just those who died at or immediately following delivery.

Five well-established formulations regarding cardiac pregnancies were outlined by Dr. Brussel:

1. The patient's heart condition must be considered carefully by both the doctor and the patient. Heart patients with no or only slight limitation of activity because of the affliction should have little difficulty in completion of pregnancy. Heart patients with moderate or marked limitation of activity can be expected to suffer grave and potentially fatal complications.

2. Women over 30 who have heart trouble should be discouraged from becoming pregnant.

3. A definite threat to successful pregnancy is auricular fibrillation, a rapid twitching of the muscular wall of the auricle instead of the regular heart beat.

4. A patient whose heart is enlarged should be warned of the possible hazard in pregnancy.

5. A woman who is troubled with high blood pressure not only does poorly during pregnancy, but after delivery frequently goes on to suffer greater hypertension.

"Every cardiac pregnancy — even the seemingly very mild case—carries a certain risk," Dr. Brussel said. "Whether that risk becomes serious trouble or is kept to a minimum depends in large part on the patient's cooperation with her doctor and careful precautionary treatment. The woman with heart disease who wants to bear children can do so now with greater expectations of success than ever before."

EDITORIALS

Cold War II

Fairfield Osborn, in his *The Limits of the Earth* (Little, Brown and Company, 1953), demonstrates the disturbing facts regarding the limited capacity of the earth as a food producer and the unlimited capacity of mankind to breed. So there are always, as a consequence, hungry peoples (now numbered at one billion).

A finite base will not support an infinitude of consumers.

By 1975, in America, there will be thirty million more than now—190 million in all. In the world at large the end of the century will see an increase of a billion.

Osborn thinks that the tension between East and West has its roots in the food question. Certainly overpopulation has been related to the last two European wars, and overpopulation still prevails in Europe—fifty million more peoples than twenty-five years ago. Of course with atomic warfare in the possible future, the story may be different.

Rationed Britain, Australia and Argentina have been significant spectacles.

As if seventy-five thousand more mouths to feed every twenty-four hours were not enough, our human society is cursed by what is nothing less than a Number Two Cold War. In addition to the Cold War between East and West we have to compete for what food we buy—those who can meet its high cost and those who can not are the competitive consumers in a nutritional rat race.

Ill fed consumers are not able to work well, whence flow many of our industrial problems.

Mental and Monetary Costs of Stress

According to Lucy Freeman *(Hope for the Troubled,* Crown Publishers, New York, 1953), mental illness "strikes down seven times as many persons in the productive years as cancer, yet we spend only one-seventh as much on research for mental illness as on cancer."

The costs in hundreds of millions of dollars of caring for mental illness in our state hospitals are bound to rise markedly because of rehabilitation programs rather than merely custodial care and also because of the increasing influx of new patients; thus there is a "net intake of 3000 additional patients each year" in just one of our state hospitals.

It is obvious that such things as the high cost of living, nutritional deficiencies and the general social unrest occasioned by the stress and strain of cold and hot wars, which power-hungry groups foster, are ruining the mental health of the populace.

This is our own view; but it is only fair to state that some of our experts think that the increase in state-hospital populations is due to man's longer life span, not

to living in the atomic age. They say that with an increase in the number of aged, many must be hospitalized for senility.

Hospital admissions are not the only way of gauging the impact of the weird social order on the mental health of the people. A lot of queer individuals either manage to evade hospitalization or do not desperately require it. Alienation is largely a matter of degree and circumstance. What gregarious man lacks some friends who are "not quite right?" In this connection one always recalls the story of the two Quaker sisters, as told by Ben Franklin: "I know not how it is, sister, but the older I get the more I find that no one is right but me and thee, and sometimes I am troubled about thee."

Mental Ills' Drag on Industry

George S. Stevenson, medical director of the National Association for Mental Health, has a point when he declares that it is not necessary to count hospital patients to find the evidence of mental illness and how widespread it is. "We need only to look at the daily papers—for any day—to find a ghastly review of the incidence of mental illness. Murder, suicide, delinquency, sex crimes, kidnapping, broken homes, alcoholism, strife, discord, unhappiness—these are the signs of mental illness and we need not look for them in hospitals or in clinics alone."

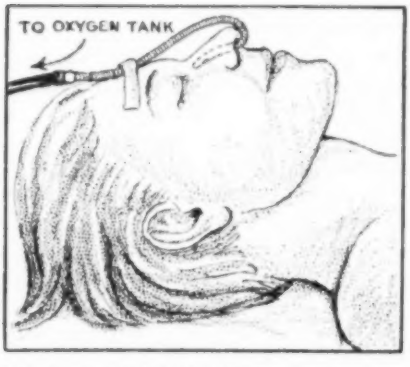
There are 650,000 patients now in mental hospitals; last year 250,000 were treated at psychiatry clinics. Dr. Stevenson's point of view is also essential in the realization that there are from 20 to 25 per cent of workers in our industrial plants and other large business organizations whose maladjustment or actual mental illness is reflected in "impaired efficiency, accident proneness, chronic absenteeism, personality clashes and habitual infraction of rules."

Fatal Snafu

Socialism in England has insured its own ultimate disaster since it not only made medical service free but also legal service. Such a law was passed in 1950. The result has been a 400 per cent increase in malpractice suits, as we pointed out in our August issue.

Here is not only a directly demoralizing factor but an indirect one in that the British citizen fails to get the full benefits of medical care, since the practitioner "avoids any act or diagnosis which will render him liable for malpractice." Yet the practitioner can not save himself entirely, as the lawsuits are on the increase despite his pathetic tactics.

Clini-Clipping



Oxygen Administration

Use of nasal catheter in the administration of oxygen (the tape binding the catheter to the nose has been omitted in order to show the position of the catheter).

PEDIATRICS

JOHN T. BARRETT, M.D.*

Coccidioidomycosis of the Bone in Children

J. Dykes and associates (*A. M. A. American Journal of Diseases of Children*, 85:34, Jan. 1953) report that in Bakersfield, Calif., 26 cases of coccidioidomycosis in children have been observed at the Kent General Hospital. Five of these cases were observed between 1909 to 1930; 4 of these 5 children died of disseminated coccidioidomycosis; the fifth patient recovered and the bone lesion healed completely. Of the 21 patients seen in 1930 to 1950, 3 died of disseminated coccidioidomycosis, and in these cases multiple bone lesions were present. Multiple bone lesions also occurred in 2 other cases. In the other cases various bones were involved; there was no site of predilection. In most cases there was a painful swelling at the site of the bone lesion and often a history of injury. In one case the bone lesion was found incidentally during an x-ray examination for another disease. The roentgenograms showed the bone lesion in these children to be osteolytic, similar to the bone lesions of coccidioidomycosis in adults. Skin tests were made in 13 of these children and were positive for coccidioidmycosis in 10 and "equivocal" in 2 cases. In adults, however, skin tests are often negative. Two of the patients with multiple bone lesions recovered, as noted above; one of these patients recently died of another disease, and a careful autopsy study showed no evidence of coccidiodomycosis. This study and the personal experience of the authors has convinced them that in regions where coccidioidomycosis is endemic, bone lesions may occur in children more frequently than has been supposed. This possibility should be suspected when osteolytic lesions occur in children, even in other regions, especially if there is a history of residence in or travel through an area where the disease is endemic. As the skin test was positive in a considerable percentage of the cases reported, this may be of aid in establishing the diagnosis and should be supplemented by a complement zxation test.

Barrett

COMMENT

This is of interest to the West coast physicians particularly. The article points out another differential diagnosis of osteolytic lesions in children. J. T. B.

Acute Cerebellar Ataxia in Children

A. Goldwyn and A. M. Waldman (*Journal of Pediatrics*, 42:75, Jan. 1953) report 3 cases of acute cerebellar ataxia in children observed within three years at a general hospital. In 2 of these cases, the ataxia which was of acute onset, was the only symptom on admission to the hospital. One of the three children had convulsions with high temperature and an upper respiratory infection on admission and developed cerebellar ataxia after these symptoms had subsided. There was a history of convulsions occurring with a feb-

* Active Staff, R. I. Hospital, Providence Lying-In Hospital, C. V. Chapin Hospital, Pawtucket Memorial Hospital; Consulting Staff, Westerly Hospital.

rile infection previously in this case. A review of the literature on cerebellar ataxia in children shows that as a rule the ataxia followed an infectious disease, as in the authors' cases. Intention tremor and nystagmus were associated symptoms in a number of the reported cases, but were not observed in any of the authors' 3 cases. As a rule the spinal fluid findings in cerebellar ataxia in children have been reported as normal; in 2 of the cases reported the cell count was increased up to 20 cells per cubic millimeter. In 2 of the authors' cases a higher cell count was demonstrated in the spinal fluid; in one case, it is noted that this pleocytosis was of short duration. The 3 patients in the authors' series made a complete recovery, the longest duration of symptoms being one month.

COMMENT

This is an interesting but not common problem. J. T. B.

The Incidence and Nature of Intracranial Calcifications After Tuberculous Meningitis

John Lorber (*Archives of Disease in Childhood*, 27:542, Dec. 1952) reports a follow-up study of 25 children who had recovered from tuberculous meningitis under treatment during a period two and half to four and a half years after beginning treatment. Radiological examination showed intracranial calcifications in 17 of these 25 children, most of which were found two to three years after the onset of the meningitis; no calcifications were found in less than eighteen months after treatment was begun. In 8 of these children the calcifications were in the brain substance; in 11 children, the calcifications were at the base of the brain, either above or above and behind the sella. These calcifications at the base of the brain were not found in any of the 10 children in whom treatment was begun in the early stage of meningitis, but they were found in 11 of the 15 children in whom treatment was begun in a later stage. Six of the 25 children studied had neurological or mental sequelae; intracranial calcifications were found in 3 of 4 children with hemiplegia and in one of the other children with residual symptoms. Since this report was completed, the addendum states, that calcifications have been found in one other child in this series forty-seven months after beginning treatment; this is the fourth child with hemiplegia. In all these patients with hemiplegia, the calcifications were basal. No significant change has been observed in any of the other children in this series, the maximum period of observation now being sixty-two months. In one child who died of tuberculous meningitis after treatment for twenty-one months, calcification of the spinal meninges was found at autopsy; and in another child, dying twenty-nine months after treatment was begun, an intracerebral calcified focus was found. The calcifications at the base of the brain which developed only in those in whom treatment was begun in the later stages of meningitis are attributed to calcification of the meningeal exudate in this area.

COMMENT

This is of interest mainly for two reasons:
1. It behooves us to diagnose and treat tuberculosis early and
2. Calcific deposits in the late posttreatment phase of the meningitis may be of some prognostic value as to the course of the patient. J. T. B.

The Effects of Magnesium Sulfate on Renal Function in Children with Acute Glomerulonephritis

J. N. Etteldorf and A. H. Tuttle (*Journal of Pediatrics*, 41:524, Nov. 1953) report a study of the effect of magnesium sulfate on the renal function of 6 children with acute hemorrhagic glomerulonephritis. All these children showed high blood pressure, 125 to 160 mm. Hg systolic pressure and 92 to 110 mm. Hg diastolic in addition to other symptoms of the disease — hematuria, albuminuria, oliguria

and edema. Magnesium sulfate was given by intramuscular injection in doses of 100 mg. per kg. body weight every four hours for eighteen to twenty hours. The glomerular filtration rate, effective renal plasma flow and tubular excretion of para-aminohippurate (Tm[PAH]) were determined in each patient before and after the administration of magnesium sulfate. In all cases the magnesium of the blood serum was increased and there was a definite fall in blood pressure, varying from 10 to 30 mm. Hg in the systolic pressure, and from 2 to 36 mm. Hg in the diastolic pressure. All the renal functions measured were reduced in these patients with glomerulonephritis. The magnesium sulfate caused no significant change in any of the functions except that effective renal plasma flow was increased, from an average of 537 cc. to an average of 635 cc. per minute. Both the reduction in blood pressure and the increase in the renal plasma flow are attributed to the "generalized arteriolar relaxation" resulting from the administration of magnesium sulfate.

COMMENT

It would appear that experimental work bears out the definite clinical impression that magnesium is effective in acute glomerulonephritis. J. T. B.

Pattern of Growth of Selected Groups of Breast-Fed Infants in Iowa City

S. L. Paiva (*Pediatrics* 11:38, Jan. 1953) reports a study of the rate and "pattern" of growth in 21 male and 24 female infants, who were breast fed from birth to the age of six or seven months. These infants were from families of "better than average" socio-economic status. A comparative study was made on a larger group of infants from families of the same socio-economic status who were artificially fed. It was found that the rate and pattern of growth were essentially the same in these two groups. These studies indicate that with modern methods of artificial feeding the known nutritional requirements of the infant born at term can be met with either breast or artificial feeding, provided that adequate supplementary feeding is given as indicated in either case. Breast feeding, however, is more desirable for most infants under normal conditions, and "should be encouraged and preferred."

COMMENT

I trust this doesn't encourage the spread of artificial feeding! We have known that most infants do perfectly well on artificial feedings —this bears it out; however, for many reasons physiologic, psychologic and economic breast feeding is to be preferred. J. T. B.

Vascular Complications of Juvenile Diabetes

H. G. Guild and associates (*Journal of Pediatrics*, 41:722, Dec. 1952) report a follow-up study of 40 patients who came under treatment for diabetes in childhood, and who had had the disease for at least ten years at the time of the last follow-up. The vascular complication most frequently found were the retinal changes that are also most specific for diabetes. Of 14 patients in whom the control of the disease had been good, 3 showed retinitis, and the patient in this group who showed the most advanced retinal changes had had severe toxemia of pregnancy before the first follow-up. Retinal changes occurred in 7 of 17 patients in whom the control of diabetes was fair, but were of marked degree in only one; retinal changes occurred in 7 of 9 patients with poor control of their disease, and in this group were "extreme and irreversible" in several cases. Renal function showed some abnormality, chiefly albuminuria, in one of the group with good control, 3 of the group with fair control and 5 of the group with poor control. It could not be definitely determined whether such abnormalities are related to the diabetes, but when they are associated with retinal changes the "presumptive evidence" indicates that they are so related. Calcification of the arteries of the legs was found in 3 of the

patients under good control, and in one of these was the only abnormal finding; it was also present in 4 of the patients under fair control and 2 of the patients under poor control. Hypertension of moderate degree was demonstrated in 8 patients, 4 in the fair control group and 4 in the poor control group. These findings indicate that vascular complications of diabetes may occur "relatively early" in juvenile diabetes but that the severity of such lesions, the time at which they occur and the rapidity of their progress is modified by the degree of control of the diabetes. In the group of patients studied it was found that good control of the diabetes was more easily maintained in children who developed the disease in early childhood (preschool age) than in those in whom the onset of diabetes occurred later. Three illustrative cases are reported.

COMMENT

Of course the aim in the treatment of diabetes is to maintain as nearly a physiological status as possible. The appearance of these complications are distressing, but seem to add further evidence that the "free diet" method of treatment is not as beneficial as good control. J. T. B.

UROLOGY

AUGUSTUS L. HARRIS, M.D., F.A.C.S.*

Anticholinergic (Banthine) Influences on Normal and Neurogenic Bladder Function

L. W. Keizur and C. V. Hodges (*Journal of Urology*, 69:259, Feb. 1953) present a study of the effect of Banthine on bladder function in normal persons and in patients with neurogenic bladder. In all these studies a 20 F catheter connected with a cystometer was used and a sterile saline solution was introduced into the bladder at a rate of approximately 50 cc. per minute. As the bladder filled, the patient was instructed to indicate the first desire to void (indicated in the pressure curve by*), the sensation of filling (indicated by F) and the onset of painful distention (indicated by P). When the pain of distention became "unbearable," the patient was instructed to void urine with "maximal" effort (indicated by M). The apparatus was then disconnected, and the bladder emptied. Bladder capacity was determined by measurement of the total volume. These cystometric measurements were first made on normal persons, then Banthine bromide was given intravenously (25 mg.); when general systemic effects of the drug became apparent, a second cystometric measurement was made. It was found that in the normal bladder, Danthine delayed the desire to void, increased the amount of bladder distention necessary to cause pain, decreased the maximal voluntary pressures and increased total bladder capacity; some residual urine also was found in normal bladders that previous to the administration of the drug had been completely emptied. Cystometric studies in patients with various

Harris

* Consulting Urologist, Middlesex Hospital, Middletown, Conn. and St. John's Episcopal Hospital, Brooklyn, N. Y. Diplomate American Board of Urology, Fellow of the American Urological Association.

types of neurogenic bladder, in addition to the study of normal bladders, showed that Banthine exerted its depressant effect on the detrusor muscle by partial blocking of the parasympathetic innervation of the bladder. On the basis of this finding, cases of neurogenic bladder must be carefully selected for Banthine therapy, since this is indicated only in those cases in which the detrusor muscle is hyperactive, i.e., in uninhibited and reflex neurogenic bladders. In 4 such cases, urinary frequency and incontinence were controlled by the oral administration of Banthine (in a dosage of 50 mg. every six hours). No serious toxic symptoms were observed with this dosage. In one case of neurogenic bladder of the reflex type, Banthine was not effective, because the external sphincter was incompetent. Bathine is definitely contraindicated in cases of hypotonic bladder.

COMMENT

Banthine, according to this author and other recent writers, has found its place in the control of urinary frequency and incontinence due to overactivity of the detrusor muscle in neurogenic bladder. Cystometric determinations have confirmed its effect in this regard. Nerve impulses are said to be blocked in the autonomic ganglia and post-ganglionic nerve. This would contraindicate its use in hypotonic bladder.

The authors only cite four cases in which oral administration of 50 mg. doses every six hours was effective. The drug appears to be well tolerated.

Austin Dodson has confirmed results in thirty patients with "uninhibited neurogenic bladder" by giving up to one hundred and fifty mg. orally four times a day. This was sometimes continued for as long as ten months. Dodson has also employed it satisfactorily as a spasmolytic for relief of pain in reno-ureteral colic, vesical tenesmus and in cystoscopic procedures.

Further studies in pharmacology will be required to provide a more complete understanding of the drug, its side-effects, potential toxicity and allergic manifestations. It should not be given in the presence of glaucoma and cardiac lesions.

A. L. H.

Staghorn Calculi

Elmer Hess and associates (*Journal of Urology*, 69:347, March 1953) present a study of staghorn calculi and the indications for treatment for patients with this type of calculi. The etiology of staghorn calculi is still not fully determined. Heredity and certain metabolic abnormalities are of significance; other factors that are of more "practical" importance include urinary stasis due to various types of obstruction in the urinary tract, which can be adequately treated, and infection. With modern chemotherapy and antibiotics, "virtually" every type of urinary tract infection can now be adequately treated, including infections due to urea-splitting organisms. In cases in which symptoms are severe and there is evidence of rapid progress of the disease, surgery is usually indicated; if the calculus is unilateral, either removal of the stone or nephrectomy may be done. Nephrectomy is in some cases the procedure of choice, especially in elderly patients, and requires a less prolonged stay in the hospital after operation. If the calculi are bilateral the best procedure must be carefully determined in each case, depending upon whether or not infection is present, the degree of destruction of the kidney parenchyma, and the severity of the symptoms. In infected cases, the chemotherapeutic or antibiotic treatment indicated is begun prior to operation and continued in the postoperative period. The Shorr aluminum hydroxide regimen is also used postoperatively. In cases where operation is not indicated, or can be delayed to determine the effects of medical management, it is desirable to determine the composition of the calculus; most of these calculi are composed chiefly of calcium phosphate, and the most effective form of medical treatment has been found to be the use of the aluminum hydroxide "routine." Most patients tolerate Amphojel in adequate dosage, 40 cc. one hour after each meal and at bedtime. This is combined with a high fluid intake. This usually results in reducing the size of the stone or preventing further growth, as shown by x-ray examinations. In the com-

paratively small number of cases in which the staghorn calculi are not composed chiefly of calcium phosphate, the use of aluminum hydroxide is not indicated, but the usual "time-honored" methods of dieting and medical treatment for certain types of stones, i.e., an alkaline ash diet and sodium citrate for uric acid stones. If there are acute flare-ups of pyelonephritis, the infection must be treated with antibiotics or chemotherapeutic agents as indicated. Otherwise, in case of more chronic, low-grade infection, no attempt is made to treat the infection while the patient is under medical management. But if surgery for removal of the stone becomes necessary, the infection is treated, as in all surgical cases. Medical management should also be employed for long periods after nephrolithotomy.

COMMENT

Nearly all of the generally accepted methods of management of staghorn calculi by urologists are embodied in this paper. The author mentions the aluminum hydroxide gels for attempted control of phosphatic calculi. Perhaps he has not sufficiently emphasized the promising possibilities confirmed by Marshall and Green. About eighteen months ago they reported that the high phosphorus intake is harmless and may be given over long periods of time. The adoption of the gel method, therefore, seems to be mandatory.

Hess does not mention hyaluronidase. Butt has obtained excellent results in prevention in nineteen out of twenty-four patients. In these, other methods had previously failed. The urinary colloidal activity is markedly increased by the injection of six hundred or more "turbidity reducing units". Further study and application of this agent will be required. Allergy and poor renal function contraindicate its use.

A. L. H.

Complications Following the Use of Streptomycin and Para-Amino-Salicylic Acid in Advanced Renal Tuberculosis

S. Scher (*British Journal of Urology*, 25:103, June 1953) reports 4 cases of advanced renal tuberculosis treated with streptomycin and PAS, in which the following complications developed after this treatment: Dilation of the upper urinary tract with reflux up the ureter, but without stricture at the uretero-vesical junction; further contraction of the bladder; stricture formation in a tuberculous ureter. Such changes occur in the natural course of events in advanced renal tuberculosis, but only slowly in a period of several years. The use of streptomycin and PAS markedly hastens the development of these complications, as shown in the cases reported; this is attributed to the fact that the treatment results in the destruction of tubercle bacilli, with liberation of toxin which produces an inflammatory reaction and resulting fibrosis. Until an effective method of preventing this reaction can be found, the author is of the opinion that streptomycin and PAS should not be used in the treatment of advanced renal tuberculosis.

COMMENT

To the knowledge and belief of the reviewer, the statements of Scher have not been confirmed by other authors. The concept that the toxins liberated by the tubercle bacilli destroyed by streptomycin and para-aminosalicylic acid, hasten marked fibrosis, stricture formation, etc., is apparently a new one.

Contrary to the present accepted methods of management of advanced renal tuberculosis, the author advises against the use of these drugs.

A recent paper by J. K. Lattimer, based on a five-year study and comprising a series of four hundred and fifty-eight cases, records favorable results with streptomycin, P.A.S. and isoniazid.

Who knows what the future will hold, good or ill, in the use of antibiotic drugs?

A. L. H.

Granulomatous Prostatitis: A Condition Which Clinically May be Confused with Carcinoma of the Prostate

G. J. Thompson and D. D. Albers (*Journal of Urology*, 69:530, April 1953) report 36 cases of granulomatous prostatitis in which the diagnosis was established by histological examination of the surgical specimen. The preoperative diagnosis was carcinoma of the prostate in 20 of these cases and benign prostatic hyper-

trophy in 16 cases. Transurethral resection was done in all these cases; the amount of tissue removed varied from 5 to 73 Gm. and averaged 22 Gm. The histologic examination in these cases showed the prostatic acini densely infiltrated with lymphocytes, plasma cells and pale-staining large mononuclear cells; foreign-body giant cells and pseudotubercles also were present around prostatic ducts. In some regions the normal structure of the prostate was completely destroyed. The transurethral resection resulted in relief of symptoms in 28 of the 36 cases; in 3 the results were "fair," and in 5 poor. One of these 5 patients died, nine days after operation, due to anuria; at autopsy "an extremely small" adenocarcinoma was found in the periphery of the prostate. None of the patients who survived operation in this series are known to have developed carcinoma of the prostate since their discharge from the hospital. In the authors' opinion there is no relationship between granulomatous prostatitis and prostatic carcinoma, though carcinoma may develop in later years, as it might in a patient with previously benign hypertrophy. The study of the clinical history and the physical findings in these cases of granulomatous prostatitis shows nothing that can be regarded as positive evidence for the differential diagnosis between granulomatous prostatitis and carcinoma of the prostate. Digital examination in granulomatous prostatitis shows that the consistency of the prostate is often the same as in carcinoma. Granulomatous prostatitis apparently occurs more frequently than has been recognized and some patients with this form of prostatitis may be treated for prostatic carcinoma by castration or hormone therapy, unless biopsy is done to establish the diagnosis. Six illustrative cases are reported.

COMMENT

The report of Thompson and Albers is significant because the type of lesion described has not been discussed in recent literature and also because the cases cited are numerous. The histopathology of lymphocytic and plasma cell invasion indicates an entity which bears no relationship to the common condition of chronic prostatitis or carcinoma.

However, the infiltrative lesions encountered may grossly be quite suggestive of malignancy. Therefore, preliminary biopsy should be made to avoid error in applying the wrong treatment.

A. L. H.

Radioactive Gold in the Treatment of Advanced Carcinoma of the Prostate and Bladder

Edgar Burns and associates *(Journal of the Louisiana State Medical Society*, 105:99, March 1953) report 24 cases of advanced carcinoma of the prostate and 4 cases of advanced bladder carcinoma treated with radioactive gold. In the cases of carcinoma of the prostate the tumor had spread into the pelvic area but metastatic lesions in bone and other structures outside the pelvis could be excluded; also all these patients were refractory to other palliative therapeutic measures. When radioactive gold was first employed, the size of the tumor was estimated as nearly as possible and 1 millicurie of gold injected per 1 cubic centimeter of tumor, i.e., 150 millicurie of gold for a tumor with an estimated volume of 150 cc. More recently smaller doses—one half to two-thirds this amount—have been employed. For infiltrating the prostatic tumor with radioactive gold, the bladder neck is exposed, as for retropubic prostatectomy, but with division of the rectus muscles close to the pubis; the bladder is opened above the internal sphincter, extending the incision into the anterior prostatic capsule when necessary. The radioactive gold is diluted to the volume necessary with normal saline, adding also 1 cc. of a 1 to 1000 solution of epinephrine and 150 turbidity units of hyaluronidase; the solution is injected to a depth of 0.5 to 1 cm., according to the thickness of the tumor, from the apex of the prostate back to the area of the internal sphincter; 1 cc. is also injected into each seminal vesicle. The bladder is closed with an

indwelling catheter. As a rule the operative wound healed promptly; there was no irradiation reaction in the bladder; the most important complication was irradiation proctitis which developed in 5 patients. Most of the patients showed some degree of leukopenia; this is controlled by frequent blood counts and transfusion as indicated. Liver function tests showed no evidence of hepatic damage. The 24 patients with advanced carcinoma of the pancreas have been treated within the last eight months; in all cases the tumor mass "almost completely disappeared" within three weeks, and it has not again increased in size in the first patient treated. A much longer period of observation is necessary to determine the true value of radioactive gold in prostatic carcinoma, but the results obtained in this series and reported by others justify continuing its use in such cases that are "otherwise incurable." In the 4 cases of bladder tumor treated with radioactive gold, good results in the disappearance of a grade III tumor, was obtained in only one case; in 2 cases there was no response, and one patient was "apparently made worse" with the development of cutaneous lesions that indicated distribution of some of the cells into the circulation.

COMMENT

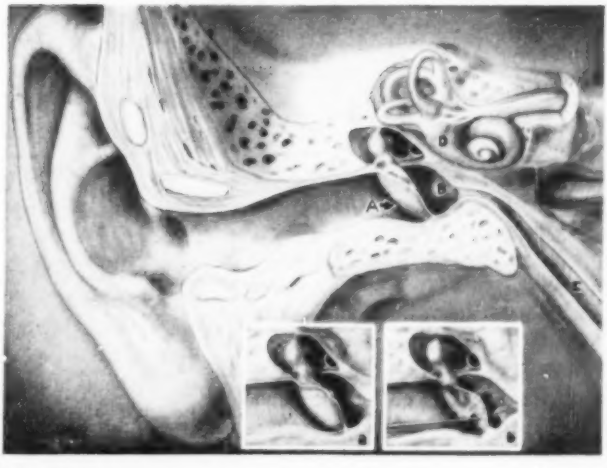
Infiltrative treatment with radioactive gold in prostatic carcinoma is a new method for patients in whom the malignancy has spread beyond the confines of the gland capsule. While it is far too soon to draw any conclusions, this and other reports of success are quite encouraging. In twenty-four cases, over an eight-month period, Burns found that the tumor mass almost completely disappeared within the first three weeks. Side-effects of irradiation proctitis and leukopenia occurred in some subjects, but did not appear to present any major problem. Bladder cancers did not yield to the treatment.

R. H. Flocks has just reported gratifying and promising results with infiltrating radioactive gold in sixty-nine patients. Radical surgical prostatectomy, however, is still the method of choice for cancer limited to the gland itself.

While C. F. Rusche has shown excellent effect in twenty-eight cases by injection of radioactive chromic phosphate, the lapse of time after treatment is too brief to determine its true effectiveness.

A. L. H.

Clini-Clipping



Anatomy of the ear showing relation of tympanic membrane A to the tympanic cavity B, the Eustachian tube C, and the labyrinth D. a—Retraction of the tympanic membrane. b—Cutting adhesions.

MEDICAL BOOK NEWS

CARDIOLOGY

Introduction to the Interpretation of the Electrocardiogram. With sixty-one plates illustrating the more important deviations from the normal, selected from the files of the Michael Reese Hospital. By Louis N. Katz, M.D., Richard Langendorf, M.D. & Alfred Pick, M.D. Chicago, University of Chicago Pr., [c. 1952]. 8vo. 78 pages, illustrated. Paper, $2.50.

It is to be hoped that this soft-covered, inexpensive book will continue to be as useful as its predecessor, *The Elements of Electrocardiographic Interpretation*, at the University of Chicago, where electrocardiography is presented to medical students as an aid in comprehending physiology of the heart.

As Dr. Carl J. Wiggers has stated, "Nature performs as good an experiment as can be obtained in the physiological laboratory".

A useful chapter is Procedure in Reading the Electrocardiogram. The illustrations are excellent and the legends are also very good.

This book can be highly recommended to the beginner, and should be very useful.

Vincent Annunziata

PSYCHIATRY

Practice of Psychiatry. By William S. Sadler, M.D. St. Louis, C. V. Mosby Co., [c. 1953]. 8vo. 1,183 pages. Cloth, $15.00.

This long and comprehensive text (over 1000 pages) is designed to give the general practitioner a wide and bird's eye view. It succeeds in being broad without being shallow. It covers an amazing area of widely divergent points of view, some of which are in sharp conflict with each other, and it does not take sides. It is a masterly job of objective reporting.

The general practitioner who wants to know just a little, not a lot, about the general differences between the varying schools of Freud, Adler, Jung, Horney, Sullivan, etc., etc. will not have to read them all. The man who wants and needs a working knowledge of the present status of shock therapy or of frontal lobotomy will not have to read a treatise. This book, written by a practicing psychiatrist, does his weeding for him. It is written in simple, understandable language. It is not written as if sacrosanct but invites disagreement and hence is valuable.

Particularly in this field, where frontiers are being pushed so fast, independent judgment is important, just as contributions from all are imperative. Psychiatry is still a broad stream and must not become a narrow, deep one, navigable by the few.

The book's weaknesses are those inherent in such an ambitious undertaking. It has a tendency to over-organize. It lists and catalogues, rather than explains. It is weakest on etiology. It often gives us words, not mechanisms. It tends to give facts, not insight nor understanding.

However, it gives valuable facts. It is both a good reference book and good reading, a rather rare combination.

Adele E. Streeseman

PATHOLOGY

Synopsis of Pathology. By W. A. D. Anderson, M.D. 3rd Edition. St. Louis, C. V. Mosby Co., [c. 1952]. 12mo. 788 pages, illustrated. Cloth, $8.00.

This author presents his material in this *Synopsis of Pathology* with utmost clarity and brevity, without sacrificing important basic fundamentals. This text does not belong to the group of elementary manuals of pathology, but rather satifies the always existent need of a good pre-

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sentation of a specialty subject for the specialists of other fields and for general practitioners.

The illustrations are excellent, the bibliography adequate, and the writing style facile. The presentation, for the major part, is by organ system affected, which makes reference easy. There are also chapters classified by etiology of disease, rather than organ involved.

This work is a most worthy companion to the author's excellent text book of *Pathology*, a larger reference work.

Edmund R. Marino

CARDIOLOGY

Electrocardiography in Practice. By Ashton Graybiel, M.D., Paul D. White, M.D., Louise Wheller, A.M. & Conger Williams, M.D. 3rd Edition. Philadelphia, W. B. Saunders Co., [c. 1952]. 4to, 378 pages, illustrated. Cloth, $10.00.

This book can be highly recommended to all, the general practitioner as well as the specialist.

It is profusely illustrated, the illustrations are very clear, and the accompanying legends are very thorough.

The new unipolar leads are thoroughly covered. All the chapters are excellent, in particular the chapter on Myocardial Infarction and the chapter on Etiologic Types.

The final section is on Electrocardiograms for Practice and Interpretation, in which the interpretations are given, followed by the clinical findings and then there is a general comment on the entire case. There are many illustrations in this chapter which are very useful to the beginner in electrocardiography.

The chapter on the Typical Normal Electrocardiogram and its Variations should also be useful to all.

This book is highly recommended for all libraries.

Vincent Annunziata

MEDICAL TIMES

THE JOURNAL OF GENERAL PRACTICE

January to December

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AUTHORS AND SUBJECTS

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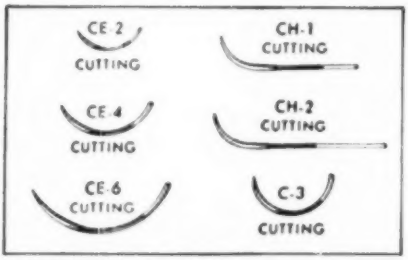
CONTEMPORARY PROGRESS

OFFICE SURGERY

SUBJECTS AND AUTHORS

EDITORIALS

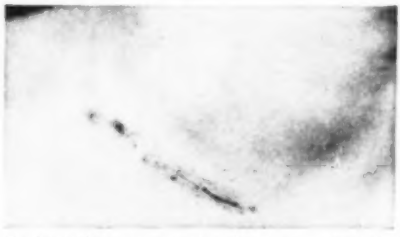
CLINICO-PATHOLOGICAL CONFERENCES



Dermalon *monofilament nylon is available on* ATRAUMATIC *needles shown above. Pliability improved if nurse moistens* DERMALON *before passing to surgeon.*

After crushing *phrenic nerve, the skin is closed with continuous subcuticular suture of 4-0* DERMALON *monofilament nylon on CE-4* ATRAUMATIC *needle. (D & G Product 1682.)*

Notice neat *approximation of skin edges obtained with* ATRAUMATIC *needle. Needles are always new and sharp. No double strand to pull through tissues.*



On the sixth *postoperative day, suture is withdrawn. Product 1682, of exceptionally smooth* DERMALON, *is very easy to remove.*

minimal scarring with D & G's DERMALON®

The patient often judges the skill of the surgeon by the degree of scarring. There is minimal scarring with DERMALON monofilament nylon suture with ATRAUMATIC® needle attached—for example, D & G's CE-4 (⅜ circle cutting edge). This was developed by Davis & Geck at the request of plastic surgeons. It is now widely used for *many types of skin closures* in major and minor traumatic surgery.

30 days later—*hardly a trace of scar, because of surgeon's delicate handling of tissues and minimal reaction to* DERMALON *suture and* ATRAUMATIC *needle.*

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in ARTHRITIS and

Like other potent therapeutic agents, BUTAZOLIDIN may sometimes produce undesirable side actions. To achieve optimal results with minimal risk of toxicity certain simple precautions are recommended:

Careful Selection of Patients excluding the senile and those with a history of peptic ulcer, drug allergy or cardiac disease.

Moderate Dosage individualized for each patient at the lowest level required to produce and maintain therapeutic benefit.

Regular Observation of Patients including careful clinical examination and periodic blood counts.

For detailed information physicians are urged to send for the brochure "Essential Clinical Data on BUTAZOLIDIN."

Bibliography

(1) Kuzell, W. C.; Schaffarzick, R. W.; Brown, B., and Mankle, E. A.: J.A.M.A. *149*:729 (June 21) 1952. (2) Byron, C. M., and Orenstein, H. B.: New York State J. Med., *53*:676 (March 15) 1953. (3) Gutman, A. B.: Am. J. Med. *13*:744, 1952. (4) Rowe, A., Jr.; Tufft, R. W.; Mechanick, P. G., and Rowe, A. H.: Am. Pract. & Digest, in press. (5) Kidd, E. G.; Boyce, K. C., and Freyberg, R. H.: Prepared for publication. (6) Steinbrocker, O.; Berkowitz, S.; Ehrlich, M.; Elkind, M., and Carp, S.: J.A.M.A. *150*:1087 (Nov. 15) 1952. (7) Currie, J. P.: Lancet 2:15 (July 5) 1952. (8) Patterson, R. M.; Benson, J. F., and Schoenberg, P. L.: U. S. Armed Forces M. J. *4*:109, 1953. (9) Stephens, C. A. L., Jr.; Yeoman, E. E.; Holbrook, W. P.; Hill, D. F., and Goodin, W. L.: J.A.M.A. *150*:1084 (Nov. 15) 1952. (10) Smith, C. H., and Kunz, H. G.: J. M. Soc. New Jersey *49*:306, 1952. (11) Davies, H. R.; Barter, R. W.; Gee, A., and Hirson, C.: Brit. M. J. 2:1392 (Dec. 27) 1952. (12) Küzell, W. C., and Schaffarzick, R. W.: California Med. 77:319, 1952. (13) Granirer, L. W.: J.A.M.A. *150*:1332 (Nov. 29) 1952. (14) Steinbrocker, O.: J.A.M.A. *151*:143 (Jan. 10) 1953. (15) Hinz, C.; Lamont-Havers, R. W.; Cominsky, B., and Gaines, L. M.: J.A.M.A. *151*:38 (Jan. 3) 1953. (16) Stifel, J. L., and Burnheimer, J.C.: J.A.M.A. *151*:555 (Feb. 14) 1953. (17) Bershof, E., and Oxman, A. C.: J.A.M.A. *151*:557 (Feb. 14) 1953. (18) Burns, J. J.; Schulert, A.; Chenkin, T.; Goldman, A., and Brodie, B.: J. Pharmacol. & Exper. Therap. *106*:375, 1952. (19) Wilkinson, E. L., and Brown, H.: Am. J. M. Sc. *225*:153, 1953. (20) Domenjoz, R.: Internat. Rec. Med. & Gen. Pract. Clin. *165*:467, 1952. (21) Delfel, N. E., and Griffin, A. C.: Stanford M. Bull., in press.

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...BUTAZOLIDIN...

(brand of phenylbutazone)

effective and potent therapeutic agent

Experience in several hundred thousand cases has now completely confirmed the therapeutic potency of the new antiarthritic agent, BUTAZOLIDIN. This entirely new synthetic, unrelated to the steroid hormones, affords these distinctive advantages:

- ***Broad Spectrum of Action*** including virtually all forms of arthritis and many other painful musculoskeletal disorders.
- ***Great Therapeutic Effectiveness*** manifested by relief of pain and functional improvement in the majority of cases.
- ***No Development of Tolerance*** leading to escape from control.
- ***Simple Oral Administration.***

Indications include gout, spondylitis, rheumatoid arthritis, osteoarthritis, and psoriatic arthritis as well as fibrositis, bursitis, and other periarticular disorders.

BUTAZOLIDIN® (brand of phenylbutazone)
Tablets of 100 mg.

Geigy

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Division of Geigy Company, Inc.
220 Church Street, New York 13, N. Y.
In Canada: Geigy (Canada) Limited, Montreal

MODERN THERAPEUTICS

Isoniazid Treatment of Tuberculosis

The Tuberculosis Chemotherapy Trial Committee of the Medical Research Council (England) reported in *Brit. Med. J.* [No. *4809*:521 (1953)] that the superiority of streptomycin and isoniazid combination over streptomycin and PAS was not great. After studying 364 tuberculosis patients they decided that none of these drugs should be administered alone. Before therapy is begun the sensitivity of the organisms should be determined and a potentially effective combination selected.

The Council found that weight gain, the lowering of temperature of pyrexial patients, and lowering of sedimentation rate was better with the combination of streptomycin and isoniazid than with streptomycin and PAS after 3 months of therapy. There was little difference in radiologic response. The proportions of patients with bacteriologically negative sputum samples after 3 months was 67 per cent for streptomycin and isoniazid, 55 per cent for streptomycin and PAS, and 37 per cent for isoniazid alone. Both combinations were effective in preventing the development of resistant strains, but where resistant strains to either one of the combination pair existed before therapy began resistance to the other often developed.

Control of Nausea of Pregnancy

The antiemetic compound, Apolamine, stopped vomiting in 88 per cent of 85 pregnant women and also eliminated the

—Continued on page 76a

FOR SPRAINS, STRAINS AND MUSCLE SPASM

a new, powerful unction

'Rubiguent' supersedes all surface applications for relief of pain by the use of the potent new penetrative agent, methyl nicotinate, in conjunction with the powerful vasodilator, histamine. Methyl nicotinate opens the way for the histamine to penetrate tissues rapidly. There it promotes prolonged, pain-relieving hyperemia, comforting analgesia and soothing warmth.

NEW

Rubiguent*

. . . for symptomatic relief of muscular aches, pains and stiffness associated with fatigue, overexertion, muscle strains, fibrositis, arthritis, neuritis, sprains . . . during physical rehabilitation following immobilization for fractures; to calm the symptoms in bronchitis and other respiratory disorders. A non-greasy, cosmetically pleasing cream, requiring only gentle surface friction for application.

*Trademark of related company

Wyeth

Philadelphia 2, Pa.

MODERN THERAPEUTICS

—Continued from page 74a

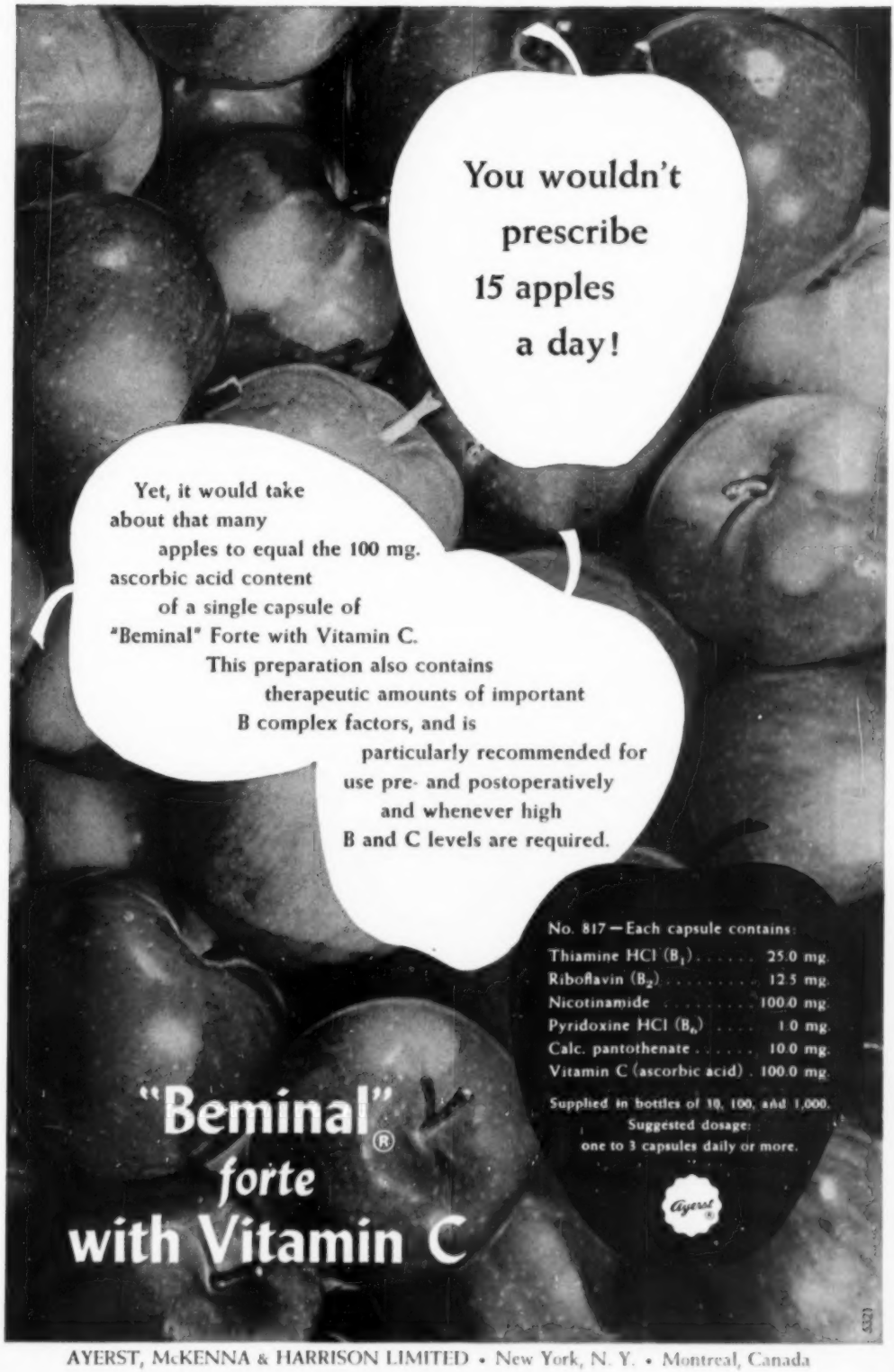
symptom of nausea in 74 per cent of the cases. All of the patients who were benefited obtained relief in less than 4 days after therapy was started, according to Cowan and Stuntz, in *J. Tennessee Med. Assoc.* [*46*:132(1953)]. The minimum dose employed was 1 tablet 3 times a day. A recurrence of symptoms was noted in 15 cases when the drug was discontinued but the symptoms disappeared again when therapy was resumed.

Chloromycetin Cleared Meningitis in Children

Chloromycetin was used in the treatment of 22 children with meningitis, 11 with influenzal meningitis, 8 with meningococcal meningitis, and 3 with pneumococcal meningitis. All of the children, ranging in age from 1 month to 4 years, responded quickly. Clinical improvement was evident within 24 to 36 hours after the drug was given. Chloromycetin hydrochloride was given intravenously in 12 patients and Chloromycetin palmitate was given orally for maintenance therapy. In the other cases oral therapy was employed exclusively.

Deane, Furman, Woodward, and Bentz stated in *Pediat.* [*11*:368(1953)] that all of the patients were able to take the oral form after the first 24 hours even though some of the cases were initially quite severe. The drug was well tolerated by the children and there were no indications of side effects.

—Continued on page 78a



AYERST, McKENNA & HARRISON LIMITED • New York, N. Y. • Montreal, Canada

MODERN THERAPEUTICS

—Continued from page 76a

A Comparison of Three Orally Administered Penicillins

The blood serum levels and the urinary excretion of liquid oral preparations of procaine penicillin G as a suspension, potassium penicillin G as a buffered solution, and N, N'dibenzylethylenediamine dipenicillin G (DDP) as a suspension were studied in 2 groups of 6 healthy adult volunteers. The subjects received the preparations on successive test days and thus served as their own controls. One group received a single dose of 300,000 units in the fasting state and the second group received a second dose in a non-fasting state.

Foltz and Schimmel reported in *Antibiotics & Chemother.* [3:593 (1953)] that both the peak serum levels and the total urinary excretion over 6 hours were significantly lower following DDP than for either of the other penicillins. More indeterminable concentrations at the 6- and 8-hour test times were obtained for DDP than for the other penicillins. Thus, it

—Continued on page 82a

Diagnosis, Please!

ANSWER

(from page 25a)

TUBERCULOMA

Circumscribed spherical nodule measuring 1½ cm. in diameter in the plane of the left 5th rib anteriorly. There is a 6mm. sized central calcification. After surgery and microscopy the nodule was found to be a tuberculoma.

They all like

pediatric

ERYTHROCIN

TRADE MARK

STEARATE

(Erythromycin Stearate, Abbott)

oral suspension

. . . the cocci-killing antibiotic for children of all ages. Tasty, stable, ready for instant use. *No mixing required*—drug retains potency for at least 18 months.

Winter infections—otitis media, bronchitis, sinusitis, pharyngitis and pneumonia—are especially sensitive to *Pediatric* ERYTHROCIN. Also, pyoderma, erysipelas, certain cases of osteomyelitis, and other infectious conditions.

Many physicians make it a practice to always prescribe *Pediatric* ERYTHROCIN when the organism is staphylococcus, because of the high incidence of staphylococcic resistance to many other antibiotics. And when the organism is resistant or when the patient is sensitive to penicillin and other antibiotics.

Pediatric ERYTHROCIN is specific in action—*less likely to alter normal intestinal flora than most other antibiotics.* Gastrointestinal disturbances are rare. No serious side effects reported.

Pediatric ERYTHROCIN can be administered before, after or with meals. Available in 2-fluidounce, pour-lip bottles. Abbott

DOSAGE

One 5-cc. teaspoonful
represents
100 mg. of ERYTHROCIN
25-lb. child • ½ teaspoonful
50-lb. child • 1 teaspoonful
100-lb. child • 2 teaspoonfuls
Every 4 to 6 hours

—Continued from page 78a

would appear that DDP does not provide a more prolonged serum level than other oral penicillin preparations. The authors also concluded that there was no evidence from their study that N,N'dibenzylethylenediamine dipenicillin G was more effective than either of the other penicillins given orally.

Single Injection of Testosterone Controls Lactation

Single intramuscular injections of 100 mg. of testosterone cyclopentyl propionate in cotton seed oil (Depo-Testosterone) were given to 125 patients during the intrapartum or early postpartum period to non-nursing mothers. The single injection proved to be an effective and satisfactory method for the control of lactation. The therapy minimized the degree and duration of pain caused by puerperal breast engorgement in the non-nursing mothers. Reporting before the A.M.A.'s sect. on obst. and gynecol. at the annual m't'g in New York, June 1-5, 1953, Drs. S. M. Dodek, J. L. Friedman, P. A. Soyster, and H. L. Marcellus stated that the results were better than obtained previously by repeated administration of estrogens and androgens.

Atabrine in Treatment of Lupus Erythematosus

Thirty-two cases of chronic discord lupus erythematosus were treated with Atabrine, given in doses of 0.1 Gm. twice daily for two weeks and then 0.1 Gm. daily thereafter for period ranging from one month to one year. All of the lesions were cleared in 12 of the patients and at least 50 per cent improvement occurred in 15 other cases. Drs. H. N. Cole, Jr., P. V. Chivington, H. N. Cole and J. R. Driver reported before the A.M.A.'s sect. on dermatol. and syphilol. at the annual meeting in New York, June 1-5, 1953, that the maximum response was obtained within 3-4 months. Two toxic reactions occurred after 3 months of treatment. Thus, the

—Continued on page 84a

Major advance in dermatitis control:

The new direct approach to the control of dermatitides is hormonal, enlisting the antiphlogistic and antiallergic potency of compound F—foremost of the corticosteroid hormones.

The new objective is adapting corticoid therapy to simple injunction treatment, and obtaining relief in various forms of dermatitides within days—sometimes within hours.

The new attainment is Cortef Acetate Ointment, which rapidly controls edema and erythema, halts cellular infiltration, arrests pruritus in such harassing skin problems as atopic dermatitis, contact dermatitis, pruritus vulvae and ani, neurodermatitis, and seborrheic dermatitis.

Cortef*

Acetate Ointment

Supplied: *Cortef Acetate Ointment is available in 5 Gm. tubes in two strengths—2.5% concentration (25 mg. per Gm.) for initial therapy in more serious cases of dermatitis, and 1.0% concentration (10 mg. per Gm.) for milder cases and for maintenance therapy.*

Administered: *A small amount is rubbed gently into the involved area one to three times a day until definite evidence of improvement is observed. The frequency of application may then be reduced to once a day or less, depending upon the results obtained.*

*TRADEMARK FOR UPJOHN'S BRAND OF HYDROCORTISONE.

A product of **Upjohn Research** *for medicine... produced with care... designed for health*

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

—Continued from page 82a

authors suggested that discontinuation of treatment after the maximum response should also reduce the toxic reactions.

Studies in Vitro on Erythromycin and Carbomycin

The spectrum of sensitive organisms to erythromycin and carbomycin was studied. It was found that both antibiotics were effective against Gram-positive staphylococci and streptococci, even though the organisms were resistant to the other major antibiotics. *Actinomyces israeli*, *C. diphtheriae*, and pathogenic *Clostridia* were also found to be sensitive to these antibiotics. However, the Gram-negative enteric bacilli, mycobacteria, and the pathogenic fungi tested were resistant.

Fusillo, Noyes, Pulaski, and Tom reported in *Antibiotics & Chemother.* [3: 581 (1953)] that resistance to staphylococci and streptococci be induced by serial transfer on media containing graded amounts of the antibiotics. They also found that there was cross resistance between erythromycin and carbomycin among the staphylococci studied.

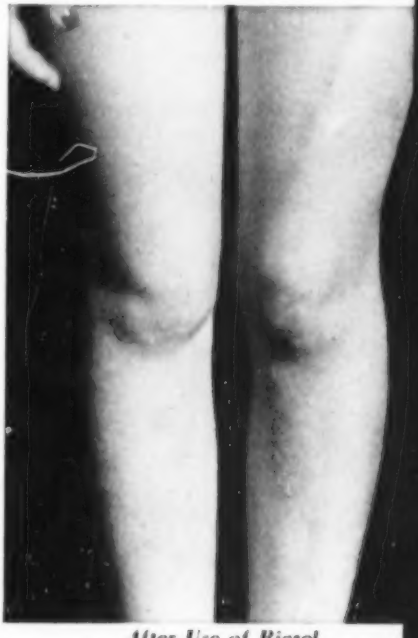
Resistance to PAS and Streptomycin in Pulmonary Tuberculosis

A series of nine patients with pulmonary tuberculosis had been previously treated with sodium or calcium *para*-aminosalicylate. Eight of the patients showed PAS-resistant strains of tubercle bacilli. These patients were placed on a regimen of 1 Gm. of streptomycin and 20 Gm. of PAS daily for at least 3 months. Five additional patients who had not received PAS previously were placed on the same regimen. After 3 months of this combined therapy 6 of the 8 patients with PAS resistant strains also had developed strep-

—Concluded on page 86a

Case Histories of PSORIASIS treated with RIASOL

Before Use of Riasol



After Use of Riasol

Statistical analysis of 21 protocols contained in a research report on the treatment of psoriasis with RIASOL revealed important facts:

All were severe cases which had failed to respond to various therapies recommended for psoriasis. The duration of the disease averaged 7.6 years, in one case 30 years.

Improvement with RIASOL was reported in 76% cases, with complete disappearance of lesions in 38%.

The average period of treatment with RIASOL before the skin patches cleared was 7.6 weeks.

Scaliness was cleared or greatly reduced by RIASOL in 71% cases.

In many cases remissions were prevented by continued use of RIASOL for weeks after disappearance of the lesions.

RIASOL contains 0.45% mercury chemically combined with soaps, 0.5% phenol and 0.75% cresol in a washable, non-staining, odorless vehicle.

Apply daily after a mild soap bath and thorough drying. A thin invisible, economical film suffices. No bandages required. After one week, adjust to patient's progress.

Ethically promoted RIASOL is supplied in 4 and 8 fld. oz. bottles at pharmacies or direct.

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Please send me professional literature and generous clinical package of RIASOL.

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RIASOL for PSORIASIS

MODERN THERAPEUTICS

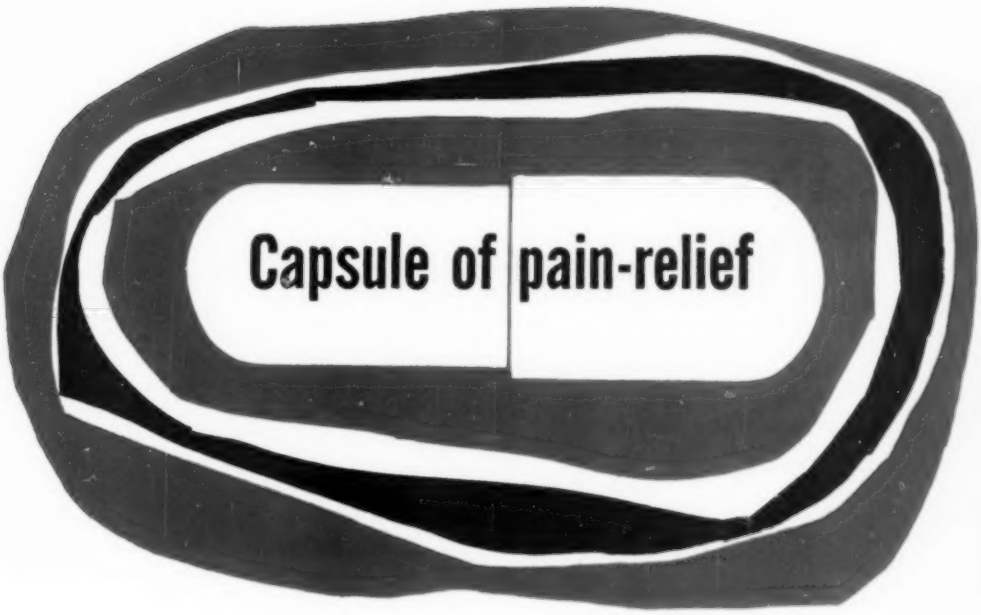
—Concluded from page 84a

tomycin-resistant strains. Within 2 more months the other 2 patients showed a like resistance. By contrast, Turnbull, Wallace, Stewart, and Crofton stated in *Brit. Med. J.* [No. 4822:1244(1953)], that only one of the 6 patients with initially PAS-sensitive strains had developed a streptomycin-resistant strain after 5 months of therapy.

The authors thus concluded that PAS, as well as streptomycin and isoniazid, should never be administered alone to tuberculous patients. They also suggested that strains which have developed resistance to PAS will not be protected from developing resistance to streptomycin when PAS is combined with streptomycin in subsequent therapy.

Chronic Leukemia Suppressed by Triethylene Thiophosphoramide

A preparation of triethylene thiophosphoramide (Thio-tepa) had been used for 6 months on 49 patients, 39 with malignant disease originating in the hematopoetic system and 10 with other inoperable malignant diseases. Most gratifying results were obtained in the chronic leukemias although promising results were also obtained in 2 patients with metastatic adenocarcinoma of the breast. However, the results with acute leukemias were not good, according to Drs. H. Shay, C. J. D. Zarafonetis, N. J. Smith, I. Woldow and D. Sun in a report before the A.M.A.'s sect. on exp. med. and therap. at the annual m't'g in New York, June 1-5, 1953. The drug was given intramuscularly or intravenously. Three patients were changed to oral administration but one responded poorly and another only fairly well. The authors pointed out that there appeared to be a reasonable margin of safety between the effective dose and the dose which will produce undue blood marrow depression. They also emphasized that, at best, the drug is only a suppressive, not a cure.



effective pain control
plus mild sedation

'Codempiral'®

Convenient dosage—two strengths

no. 2 Each capsule contains:

Codeine Phosphate	gr. ¼
Phenobarbital	gr. ¼
Acetophenetidin	gr. 2½
Aspirin	gr. 3½

no. 3 Each capsule contains:

Codeine Phosphate gr. ½
plus the other
ingredients listed above

Both strengths available in bottles of 100

Subject to Federal Narcotic Law

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NEWS AND NOTES

Emotions and Tensions are Frequent Causes of Headaches

When something bothers a turtle, he pulls his head into his shell. When something bothers a human being, he pulls his head into the shell of a headache.

A headache is not a disease by itself, but rather a symptom of a disease or functional disturbance. Headaches of emotional or psychogenic origin are extremely common.

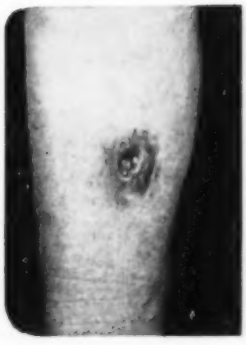
"The emotional, fidgety person besieged by worry, anxieties and fatigue often suffers from headaches," Dr. Fabricant wrote in a recent *Today's Health* magazine, published by the A.M.A. "In many instances he is not aware of the underlying difficulty for precipitating the head pain."

Emotional headaches can be fickle and bizarre. They have no pattern as to time, duration of attack or location of pain, Dr. Fabricant pointed out. There is often a tendency of the patient to exaggerate the extent of the headache, to portray it in melodramatic terms and to boast of the suffering he is compelled to endure. However, such headaches rarely interfere with work, play or sleep, and are usually relieved by a brief nap or an aspirin. These headaches may go on for years without seriously impairing vigor or well-being.

"In many people with chronic headaches, medication is chiefly of value in relieving the discomfort of the acute attack. But, only by reducing the amount of mental stress can headaches be reduced in frequency and severity and thereby rendered easier to control by therapeutic means."

—Continued on page 90a

varicose ulcer



FEBRUARY 11
2.1 x 1.3 cm. varicose ulcer, unresponsive to previous therapy.

FEBRUARY 19
Epithelial ingrowth from margins after 8 days' therapy with MY-B-DEN, Sustained-Action, 20 mg.

MARCH 19
Ulcer completely healed. Patient received 22 injections of MY-B-DEN, Sustained-Action, 20 mg. (1 cc. I. M.)

clinical demonstration of response to

MY-B-DEN®

(adenosine-5-monophosphate)

NONTOXIC, SYSTEMIC MUSCLE ADENYLIC ACID THERAPY

The complications of chronic venous insufficiency respond dramatically to MY-B-DEN. Itching, edema, pain, and burning are quickly relieved and "the ulcer proceeds to heal."[1] The benefits of supportive measures are enhanced, and when surgery is indicated MY-B-DEN is a "valuable adjunct."[2]

Administration: 1 cc. injected intramuscularly 3 times weekly. For severe cases dosage treatment may require 4 to 6 weeks.

Supplied: MY-B-DEN Sustained-Action in gelatin solution: 10 cc. vials in two strengths, 20 mg. per cc. and 100 mg. per cc. adenosine-5-monophosphate as the sodium salt. (Also available in Aqueous Solution and Sublingual Tablets.)

1. Rottino, A.; Boller, R., and Pratt, G. H.: Angiology *1*:194, 1950.

2. Boller, R.; Rottino, A., and Pratt, G. H.: Angiology *3*:260, 1952.

"Pioneers in Adenylic Acid Therapy"

Bischoff

ERNST BISCHOFF COMPANY, INC.
IVORYTON, CONNECTICUT

NEWS AND NOTES

—Continued from page 88a

However, Dr. Fabricant stressed, headaches of recent origin frequently require immediate investigation as they may indicate the beginning of a serious ailment. A thorough clinical and laboratory study will determine whether or not a disease is present.

National Foundation Fellowships

The National Foundation for Infantile Paralysis announces the availability of a limited number of additional postdoctoral fellowships to candidates whose interests are research and teaching in medicine and the related biological and physical sciences. The purpose of these National Foundation fellowships is to increase the number of professional workers qualified to give leadership in the solution of basic and clinical research problems including those of poliomyelitis and other crippling diseases.

The fellowships cover a period of from one to five years. Stipends to Fellows range from $3,600 - $7,000 a year, with marital and dependency status considered in determining individual awards. Institutions which accept Fellows receive additional compensation for expenses incurred in relation to their training programs.

Eligibility requirements include United States citizenship (or the declared intention of becoming a citizen), sound health and an M.D., Ph.D., or an equivalent degree.

Selection of candidates is made by a Fellowship Committee composed of leaders in the fields of medical research and professional education. The designation "Fellow of The National Foundation for Infantile Paralysis" will be given to successful candidates.

A total of 181 fellowship awards in these categories has been made by the National Foundation up to August 1, 1953.

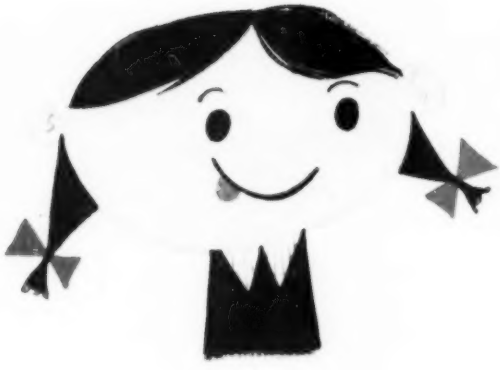
—Continued on page 92a

Taste Toppers . . . for all ages

that's what physicians and patients alike call these two favorite dosage forms of Terramycin because of their unsurpassed good taste. They're nonalcoholic — a treat for patients of all ages, with their pleasant raspberry taste. And they're often the dosage forms of first choice for infants, children and adults of all ages.

Terramycin®

BRAND OF OXYTETRACYCLINE



Pediatric Drops

Each cc. contains 100 mg. of pure crystalline Terramycin. Supplied in 10 cc. bottles with special dropper calibrated at 25 mg. and 50 mg. May be administered directly or mixed with nonacidulated foods and liquids. Economical 1.0 gram size often provides the *total dose* required for treatment of infections of average severity in infants.

Supplied: Bottles of 1.0 Gm.

Oral Suspension *(Flavored)*

Each 5 cc. teaspoonful contains 250 mg. of pure crystalline Terramycin. Effective against gram-positive and gram-negative bacteria, including the important coli-aerogenes group, rickettsiae, certain large viruses and protozoa.

Supplied: Bottles of 1.5 Gm.

Pfizer

PFIZER LABORATORIES, *Brooklyn 6, N. Y., Division, Chas. Pfizer & Co., Inc.*

NEWS AND NOTES

—Continued from page 90a

Complete information concerning qualifications and applications may be obtained from: Division of Professional Education, The National Foundation for Infantile Paralysis, 120 Broadway, New York 5, New York.

85% Cures With New Pinworm Drug

At the recent meeting of the American Academy of Pediatrics in Miami a scientific exhibit was presented by Dr. Thomas S. Bumbalo and Dr. F. J. Gustina, of the University of Buffalo, on the treatment of pinworm infestations in children. Pinworms occur in about 40% of the white population under twenty years of age and 10% of the negro population under twenty in the United States, according to Dr. Bumbalo. The results of treatment with several drugs were shown. The newest of these is 'Antepar' Citrate brand Piperazine Citrate, a drug of low toxicity and marked anthelmintic properties. Dr. Bumbalo and Dr. Gustina obtained 85% cures with piperazine and observed no side reactions of any kind.

The drug is a pleasantly flavored syrup containing the equivalent of 100 mg./cc. of piperazine hexahydrate and is marketed by Burroughs Wellcome & Co. (U.S.A.) Inc. under the name of Syrup of 'Antepar' Citrate brand Piperazine Citrate.

Volvulus of Sigmoid Colon, Diagnosis and Treatment

E. J. Krol and F. B. Tabaka at the 1953 meeting of the International Academy of Proctology stated that volvulus of the sigmoid colon rarely occurs in North America, but it must nevertheless be considered as a posibility in the diagnosis of acute intestinal obstruction. In the United States 1 to 4 per cent of all cases of intestinal obstruction are due to volvulus of the sigmoid, according to reports from different hospitals. The condition occurs most frequently in middle-aged and elderly patients, and more often in men than in women. The etiology of volvulus

of the sigmoid has not been definitely determined. Factors that predispose to this type of volvulus include the presence of an elongated, freely movable sigmoid colon, an elongated mesosigmoid or short attachment of the mesosigmoid, adhesions of the sigmoid colon, increased peristaltic activity, due to drugs or "violent" purgatives. In the opinion of the authors there is a disturbance in the peristaltic action, gas and fluids being propelled into the lumen of the bowl segment involved, while there is absence of reverse peristalsis and inability to remove gas and fluids proximally. In the acute stage of volvulus of the sigmoid, the symptoms are cramp-like pains, localized primarily around the umbilicus or in the left lower quadrant; rapid and severe distention of the sigmoid; inability to empty bowels, although there is an urge to defecate; rapid pulse and respiration, nausea and vomiting are later rather than early symptoms. X-ray examination shows the distention of the sigmoid loop and the Frimann-Dahl sign (the sides of this dilated sigmoid loop forming three lines that converge toward the site of obstruction). If the characteristic signs are not found on the flat plate, the use of a barium enema may be necessary for diagnosis. In some cases, especially in older patients, there may be less acute symptoms, a history of previous attacks and more gradual onset of attack of constipation with cramping abdominal pain and distention, which may be relieved by defecation with copious stools. In such a subacute stage and in the very early stage of an acute attack, the volvulus may be relieved by the use of a tube passed through the proctoscope or sigmoidoscope. When this is not possible, immediate operation is indicated; blood transfusion, electrolytes and fluids and antibiotics and chemotherapy are used as indicated. The operation of choice is primary resection of the involved segments with end-to-end or end-to-side anastomosis. In bad risk

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patients, the Bloch-Mikuliez resection with colostomy can be done. The best anesthetic is cyclopropane, with 10 per cent cocaine, if there is marked distention; or with pentothal sodium if the patient is "decompressed."

Criteria for Hair Care An Individual Problem

Wash that dirt right out of your hair.

Washing the hair per se will not result in hair damage, a medical consultant wrote in a recent *Journal of the American Medical Association*. But, if strong cleansing agents are used consistently, the hair and scalp may become excessively dry.

"Years ago, cleansing agents were more often alkaline than they are today, and inferior shampooing results were not rare.

"There are few persons who find it necessary to wash the hair more than twice a week. The average person in a city may require shampoos once a week. Wetting the hair for grooming purposes is not harmful.

"The type of detergent used in a particular shampoo is a trade secret, unless the manufacturer wishes to disclose it. Some shampoos contain both a soap and a synthetic detergent product. The most satisfactory criterion for determining shampoo action is to experiment with several reputable brands until one is found that suits the individual needs. This experimentation will not result in serious hair damage. The most that will occur is temporary excessive dryness and such cosmetic disadvantages as inferior manageability and hair gloss.

Antimalarial Drug Aids in Treatment of Skin Disease

Preliminary studies have shown chloroquine diphosphate, an antimalarial drug, to be of value in the treatment of a serious

skin affliction, discoid lupus erythematosus, according to an article in a recent *Journal of the American Medical Association.*

Discoid lupus erythematosus is a superficial inflammation of the skin marked by disk-like patches with raised reddish edges and depressed centers, and covered with scales or crusts. These fall off leaving dull-white scars.

Results of a four-month study of 14 patients suffering from the affliction who were treated with the drug were described by Drs. Leon Goldman, Donald P. Cole and Robert H. Preston, Cincinnati. Great improvement was noted in nine patients and some improvement in three; there was no change in the condition of two patients.

Although some toxic effects to chloroquine were noted, they were less than those of other antimalarial agents which have been used successfully to treat the condition ,the doctors stated, adding:

"Preliminary clinical trials have shown chloroquine diphosphate to be of value in the treatment of the chronic discoid phase of lupus erythematosus. This antimalarial agent is less toxic than quinacrine (Atabrine), but, with prolonged administration, the possibility of the occurrence of toxic symptoms must be considered."

TB Drug Aids in Treatment of Serious Fungous Infection

Isoniazid, a drug which has been used to treat tuberculosis, has proved of value in the treatment of actinomycosis, according to Drs. Leon V. McVay, Jr., and Douglas H. Sprunt, Memphis, Tenn.

Actinomycosis, although a fungous infection, is similar in many respects to tuberculosis. Producing lesions of the bone or lung, the disease has a very high morbidity and mortality rate. It usually is acquired through the handling of infected cattle.

Three cases in which patients afflicted with actinomycosis recovered following isoniazid therapy were described by the

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doctors in a recent *Journal of the American Medical Association.*

The patients received approximately five times the amount of isoniazid that has been given to patients suffering from tuberculosis. No significant side-effects to the drug were noted during the four to ten week periods the drug was administered, the doctors stated, adding:

"Whether a more prolonged course of therapy would have resulted in increased toxicity is uncertain. Obviously, until more is known concerning isoniazid, patients receiving such dosage should be carefuly observed.

"It is realized that the follow-up periods in the three cases reported in this study are quite brief and that prolonged observation is necessary. However, the studies and initial clinical results indicate that isoniazid is of value in the treatment of actinomycosis."

Eating Unripe Persimmons May Cause Stomach Mass

Eating young, unripe persimmons may result in the formation of a ball-like mass in the stomach requiring surgical removal. The mass, called a diospyrobezoar, is the result of the persimmon seeds lodging and swelling in the gastrointestinal tract.

Fourteen such cases were reported by Dr. Charles M. O'Leary, Oklahoma City, in a recent *Archives of Surgery*, published by the A.M.A.

Dr. O'Leary said diospyrobezoars are found predominately in males, principally farmers. High gastric acidity was very prevalent in most persons so afflicted, and although the majority of patients were in the later decades of life, the age range was from 2 to 78 years.

The initial symptoms of a diospyrobezoar are dependent upon the degree of gastric irritation. Within 24 hours after ingestion of the fruit, most patients have acute abdominal symptoms characterized by abdominal pain, tenderness, nausea and vomiting. In a few days the acute

symptoms subside and are followed by the appearance of an abdominal mass. Weight loss and alternating constipation and diarrhea also may occur.

Symptoms become severer in the later course of the disease. This is due either to an uncomplicated gastric ulcer, to a gastric ulcer with complications, or to acute intestinal obstruction, he added. Of the 14 cases reported by Dr. O'Leary, 10 had a gastric ulcer; three patients died.

Minor Surgery Relieves Varicose Veins—Exercise May Prevent Them

Minor surgery permanently relieves nine out of ten cases of varicose veins—but simple exercises may prevent them.

Anyone can have varicose veins, although they are usually found in a person who has a job that keeps him on his feet all day, especially a job that involves more standing than walking.

Whenever a vein in the lower leg is bigger than a lead pencil, medical treatment should be sought, Dr. Eichenlaub wrote in a recent *Today's Health* magazine, pub-

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NEWS AND NOTES

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lished by the *A.M.A.*

"Varicose veins slow up the circulation in the legs and let waste products pile up in the muscles of the feet and calves, causing an extreme feeling of tiredness, which goes on to severe muscle cramps.

"Varicose veins, with their ugliness, the discomfort they cause and the chance of eczema, ulcers or bleeding which goes along with them, should certainly be prevented if possible. But if they aren't prevented, they should at least be treated early."

A simple corrective procedure consists of tying off the surface vein system of the leg where it enters the bigger veins, and making each branch clot by a series of injections of chemicals into them. This operation "gives good results at least nine times out of ten," he added. However, if this procedure fails to provide relief, more extensive operative treatment may be taken.

"There is one other approach to the varicose vein problem," Dr. Eichenlaub pointed out. "During World War II, the army taught many of its recruits a leg exercise that was aimed at cutting foot fatigue. In the middle of each long hike, the soldiers were told to take off their shoes and socks, lie on their backs with their feet high above them, and jiggle their feet rapidly with the muscles relaxed. This exercise flushed out the veins and washed waste products out of the muscles.

"The same exercise would save many people from developing varicose veins if it were done whenever their feet and legs felt tired. Tired feet and legs usually mean congested veins. Both the tiredness and the congestion can be helped by this simple exercise. If congestion is never allowed to stretch the veins until their valves do not work, varicose veins will never develop."

Urge Public Realization of Coroner's Office Welfare Role

The general public must be educated to realize the important role a well functioning medical coroner's office plays in their welfare, it was stated in a recent issue of *A.M.A. Journal*.

Cooperation of the public with the local coroner's office will provide many benefits to the entire community, in the opinion of Drs. Kurt E. Landé and Garrett Boone, Hamilton, Ohio. These benefits include the discovery of the major causes of death, the detection of epidemics, the uncovering or disproof of homicides and the determination of causes of accidents which result in death.

"The preponderance of coroner's cases were sudden deaths from natural causes," the doctors stated. "This is also the group in which the largest number of autopsies were performed; this incidence is similar to that of the whole country. Heart disease, mainly the direct or indirect sequelae of coronary arteriosclerosis, is by far the leading cause of sudden, unexpected death.

"Accidents are the next most important group of coroner's cases, with automobile accidents the commonest. Railroad accidents, however, are, in this country, far from rare and are frequently the result of unprotected railroad crossings at which drivers or pedestrians either half asleep and/or intoxicated are caught by a train. Industrial accidents are encountered in the usual frequency, in spite of existing safety programs in the steel and paper mills, machine tool factories, and foundries.

"Although true homicides have been infrequent, suicides are fairly common; among them have been several homicide-suicide situations. Too many sleeping pills, gunshot wounds, and carbon monoxide are employed more often than hanging."

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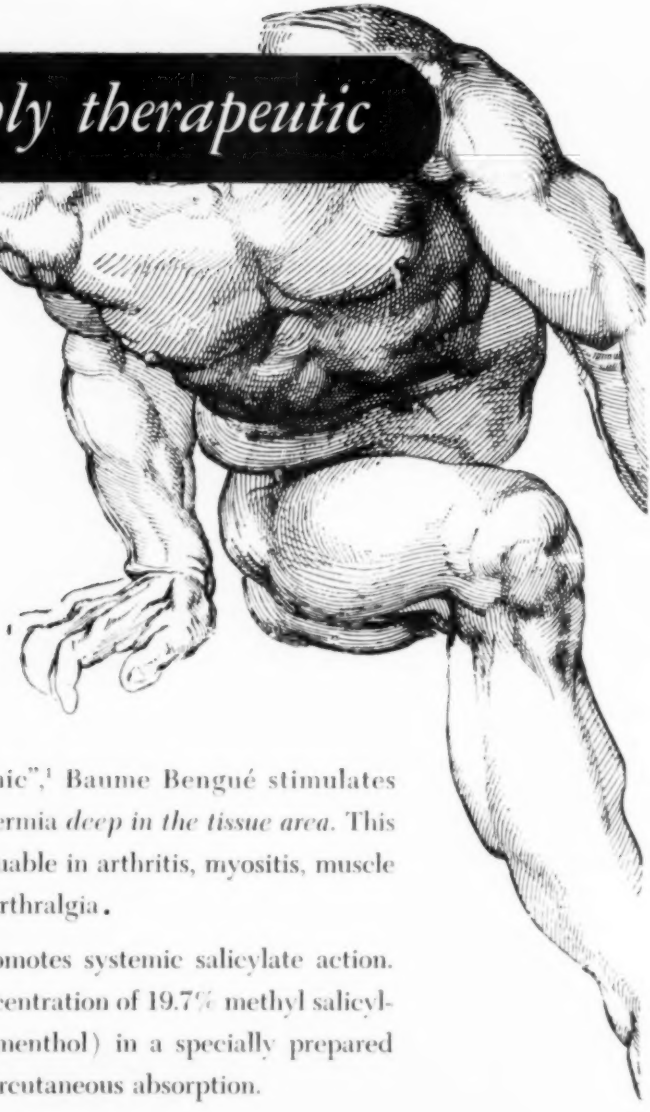

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1. Lange, K., and Weiner, D.: J. Invest. Dermat. 12:263 (May) 1949.

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